

Product-Chemical Profile for Nail Products Containing Toluene

Discussion Draft – March 2019

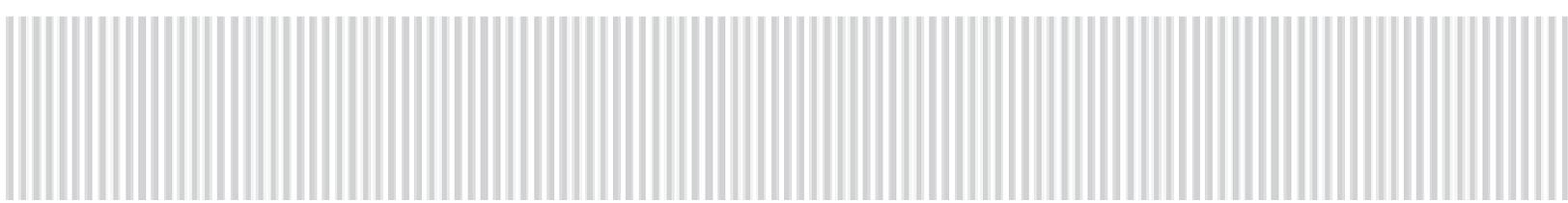


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ABOUT THIS PROFILE

The Department of Toxic Substances Control (DTSC) identifies product-chemical combinations for consideration as Priority Products in accordance with the process identified in Article 3 of the Safer Consumer Products (SCP) regulations.¹ DTSC finds toluene in nail products meets the key prioritization criteria² for listing a Priority Product:

- (1) There must be potential public and/or aquatic, avian, or terrestrial animal or plant organism exposure to the Candidate Chemical(s) in the product; and
- (2) There must be the potential for one or more exposures to contribute to or cause significant or widespread adverse impacts.

The SCP regulations allow DTSC to use a narrative standard to show how these criteria are met. This Product-Chemical Profile (Profile) provides that narrative, demonstrating that the regulatory criteria have been met and serving as the basis for Priority Product rulemaking. The Profile does not provide a comprehensive assessment of all available adverse impact and exposure literature on toluene or nail products. DTSC will finalize this Profile after considering public comments and may then start the rulemaking process. If this Priority Product regulation is adopted, the responsible entities must follow the reporting requirements pursuant to the SCP regulations.³

Readers should consider the following:

1. This Profile is not a regulatory document and does not impose any regulatory requirements.
2. The Profile summarizes information compiled by DTSC as of March 2019.
3. DTSC requests that stakeholders provide data on the chemical and product described in this document to assist us in the discernment process that may lead to our regulatory proposal. Written comments can be submitted using our information management system, CalSAFER,⁴ prior to March 15, 2019.
4. By proposing to list this product-chemical combination as a Priority Product containing a Chemical of Concern, DTSC is not asserting that the product cannot be used safely. The proposal indicates only that there is a potential for exposure of people or the environment to the Chemical of Concern in the Priority

Candidate Chemical: A chemical that exhibits a hazard trait and is listed on one or more authoritative lists in the SCP regulations

Product-Chemical Profile: A report generated by DTSC to explain its determination that a proposed Priority Product meets the SCP regulatory criteria for potential significant or widespread adverse impacts to humans or the environment

Priority Product: A product-chemical combination as identified in regulation by DTSC that has the potential to contribute to significant or widespread adverse impacts to humans or the environment

¹ CAL. CODE REGS. tit. 22, Division 4.5, Chapter 55, Article 3

² CAL. CODE REGS. tit. 22, § 69503.2(a)

³ CAL. CODE REGS. tit. 22, § 69503.7 and Article 5 (Alternatives Analysis)

⁴ <https://calsafer.dtsc.ca.gov/>

Product; that such exposure has the potential to cause or contribute to significant or widespread adverse impacts; and that safer alternatives should be explored.

SUMMARY OF THE RATIONALE FOR PRODUCT-CHEMICAL SELECTION

DTSC proposes to identify nail products containing toluene – including nail coatings and nail polish thinners – as a Priority Product with a Chemical of Concern. Toluene, formaldehyde, and dibutyl phthalate (DBP) have been historically called the “toxic trio” when used together in nail products. While nail product manufacturers have largely phased out use of formaldehyde and DBP, some nail products still contain toluene.

The U.S. Food and Drug Administration (FDA) has limited regulatory oversight of cosmetics and personal care products, including nail products. The FDA does not have the authority to require safety testing of cosmetics, and there is no approval process for cosmetics and personal care products prior to sale in the U.S. (except for color additives). Further, there is no legal requirement to report adverse impacts related to cosmetics and personal care products, and the FDA has no recall authority over such products.

Toluene is a solvent used in a variety of formulated products including nail products. It is a liquid at room temperature and readily volatilizes into air. Toluene exhibits several health hazard traits and appears on nine of the 23 authoritative lists that make up the Candidate Chemicals List in the SCP regulations. Exposure to toluene has the potential to cause or contribute to adverse human health impacts, including:

- **Nervous system effects.** Neurotoxicity is a critical human health concern following acute, intermediate, or chronic toluene exposure.
- **Developmental toxicity.** Toluene exposure is linked to adverse effects in developing fetuses and has the potential to cause birth defects.
- **Respiratory, liver, and kidney toxicity.** Toluene exposure has been linked to harm to the respiratory tract, the liver, and kidneys.
- **Immune system, vision, and hearing effects.** Toluene exposure is also linked to adverse impacts to the immune system and vision and hearing impairment.

The primary exposure route from nail products is vapor inhalation. Toluene has been detected in air in nail salons at levels above California regulatory standards, and nail technicians (also known as manicurists) have an especially high potential for exposure.

Use of nail products in salons and at home has the potential to expose nail technicians, other salon workers, patrons, and nail product consumers to toluene. The primary exposure route from nail products is vapor inhalation.⁵ Toluene has been detected in air in nail salons at levels above California regulatory standards, and

⁵ Toluene exposure can also occur through dermal application of products and orally from accidental ingestion and hand-to-mouth behavior.

nail technicians (also known as manicurists) have an especially high potential for exposure. The magnitude of toluene exposure can be affected by several factors:

- **Ventilation.** Nail salons often have inadequate ventilation.
- **Length of the work day.** Salon workers often work more than eight hours per day and 40 hours per week.
- **Availability of information.** Salon workers are often not given adequate information on chemical safety. If Safety Data Sheets are available, workers may have difficulty reading and understanding them, especially if English is not their native language.
- **Use of personal protective equipment.** Salon workers are often not provided with proper personal protective equipment such as nitrile gloves and half-facepiece air purifying respirators with organic vapor filtering cartridges that can reduce exposure to toluene and the resulting adverse impacts.
- **Other factors.** Building size, room dimensions, air exchange rates, and weather conditions also influence the degree of toluene exposure in nail salons and at home.

Nail industry workers' exposure to chemicals is an environmental justice issue. In California, most nail technicians are Vietnamese immigrants of low socioeconomic status and are often women of childbearing age.

Fetuses, infants, and children represent another group that is especially vulnerable to toluene exposure from nail products. Due to physiological differences, infants and children are more susceptible to adverse impacts from toluene exposure than adults. Nail technicians who work while pregnant risk exposing their fetuses to toluene in the womb. Toluene has been detected in breast milk, and nursing mothers who work in nail salons can expose their infants when they breastfeed. Salon workers who bring their infants and children to work may expose them to toluene vapors present in indoor air.

Nail products and professional manicure/pedicure services are popular in the United States. In California alone, there are over 9,000 nail salons and more than 130,000 licensed manicurists. Nail products, including ones containing toluene, are also widely used at home. Retail sales of nail products exceed \$1 billion per year in the U.S. In 2015-16, nail polish sales represented \$741 million of this amount.

Nail industry workers' exposure to chemicals is an environmental justice issue. In California, most nail technicians are Vietnamese immigrants of low socioeconomic status and are often women of childbearing age.

Based on these factors, DTSC has determined that toluene-containing nail products may contribute to or cause significant or widespread adverse impacts to nail industry workers, women, infants, children, and environmental justice communities; thus, DTSC proposes to identify nail products containing toluene as a Priority Product.

1 PRODUCT-CHEMICAL DEFINITIONS AND SCOPE

This Section introduces the Candidate Chemical(s) and the product that constitute the proposed product-chemical combination.

1.1 Scope of Candidate Chemical

Toluene, Chemical Abstract Service (CAS) Registry Number 108-88-3

Synonyms (ATSDR 2017; HSDB 2016)

- Methylbenzene
- Phenylmethane
- Benzene, methyl-
- Toluol
- Methylbenzol

Registered trade names (ATSDR 2017; HSDB 2016)

- Methacide
- Antisal 1A

Molecular Formula: $C_6H_5CH_3$ or C_7H_8

Toluene is a clear, colorless, flammable volatile liquid that has a sweet and pungent odor. Toluene is produced in the process of making gasoline and other fuels from crude oil and in making coke from coal (ATSDR 2015; ATSDR 2017). Toluene is used as a solvent in a variety of nail products such as nail polish, nail hardeners, polish removers (FDA 2017), and nail polish thinners. Historically, toluene was used as a solvent in nail polish removers, but this use is now effectively banned by the California Air Resources Board (CARB) Consumer Products regulations, which limit the total concentration of volatile organic compounds in polish removers to 1 percent by weight (CARB 2015; CARB 2017; Wolf 2016).

Toluene is listed as a Candidate Chemical based on the following:

- Identified as a toxic air contaminant by CARB (CARB 2011).
- Identified on the Centers for Disease Control and Prevention's Fourth National Report on Human Exposure to Environmental Chemicals and Updated Tables (CDC 2017).
- Identified with noncancer endpoints and listed with an inhalation reference exposure level by the California Office of Environmental Health Hazard Assessment (OEHHA) under Health and Safety Code section 44360(b)(2) (OEHHA 2016).
- Listed as a developmental toxicant under Proposition 65 (Safe Drinking Water and Toxic Enforcement Act of 1986) (OEHHA 1991).

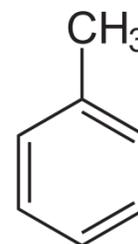


Figure 1. Chemical structure of toluene (HSDB 2016)

- Identified as a chemical for which a primary Maximum Contaminant Level (MCL) has been established and adopted under section 64431 or section 64444 of chapter 15 of title 22 of the California Code of Regulations (SWRCB 2014).
- Identified as a priority toxic pollutant in California Water Quality Control Plans under section 303(c) of the federal Clean Water Act and in section 131.38 of title 40 of the Code of Federal Regulations, or identified as pollutants by California or the U.S. Environmental Protection Agency (U.S. EPA) for one or more water bodies in California under section 303(d) of the federal Clean Water Act and section 130.7 of title 40 of the Code of Federal Regulations (SWRCB 2012; U.S. EPA 2000).
- Identified as a neurotoxicant in the Agency for Toxic Substances and Disease Registry's Toxic Substances Portal (ATSDR 2011).
- Identified as a chemical for which a reference dose or reference concentration has been developed based on neurotoxicity in U.S. EPA's Integrated Risk Information System (U.S. EPA 2005a).

1.2 Scope of Product

The scope of this proposal covers nail products containing toluene, including:

- nail coatings, and
- nail polish thinner.

This proposed product-chemical combination includes the following toluene-containing nail products, as defined below.

"Nail coatings" means any clear or colored paint, polish, lacquer, enamel, or gel product marketed or sold for application to the fingernails or toenails. Subproducts include nail polish, lacquers, enamels, base coats, undercoats, top coats, gel nails, gel nail polish, Shellac, hard gel, nail art, and airbrush nail art paint.

- "Nail polish" is a varnish or paint applied to the fingernails or toenails to color them or make them shiny.
- "Lacquer" or "enamel" is a coating that dries by means of solvent evaporation.
- "Base coat" or "undercoat" is a clear or milky-colored coating that is used before applying other coatings to the nail. It may be marketed for strengthening or protecting the nail, restoring moisture to the nail, or helping other coatings to adhere to the nail.
- "Top coat" is used after applying other coatings to the nail. It may be marketed for the use of protecting underlying coatings or to add shine, gloss, or matte to the nail.
- "Gel" or "UV gel" or "nail gel" is a pre-mixed coating that is hardened using an ultraviolet (UV) or light-emitting diode (LED) lamp.
- "Gel nail polish" or "gel polish" is a gel varnish coating with a look and feel similar to UV gel but which may not require UV or LED lamp heat to dry. Gel polish typically contains color but can also be a clear nail coating.
- "Shellac" is the brand name for a nail product created by Creative Nail Design. It is a hybrid which is a combination of nail polish and gel. Shellac is applied directly onto natural nails, and it is cured through UV light.

- “Hard gel” is a nail enhancement that can be sculpted and shaped like acrylic nails, but hardens through UV or LED light rather than through evaporating solvents.
- “Nail art” means any technique of decorative art applied to fingernails and/or toenails including various overlays of nail polish, UV gel, or hybrid coatings like Shellac or airbrush paint. This definition only includes nail art that falls within the definition of “nail coatings.”
- “Airbrush nail art paint” is a coating that is sprayed onto the nail by a device using compressed air. This product may also be labeled ink, polish, paint, or pigment for airbrush nail art.

“Nail polish thinner” means any liquid product that is marketed or sold for the use of reducing viscosity of nail coatings. It may be marketed for the use of increasing the fluidity or restoring the consistency of nail coatings.

Nail coatings include, but are not limited to, products that can be categorized by Global Product Classification (GPC) identified by the following codes (GS1 2017):

- Segment: 53000000 – Beauty/Personal Care/Hygiene
 - Family: 53160000 – Cosmetics/Fragrances
 - Class: 53161200 – Nail Cosmetic/Care Products
 - Brick: 10000360 – Cosmetics – Nails (nail coatings)
 - Brick: 10000359 – Nails – False
 - Attribute: 20000292 – Type of False Nails
 - Value: 30004466 – FALSE NAILS UV GEL
 - Attribute: 20000794 – Type of Material
 - Value: 30004342 – UV ACTIVATED GEL

1.2.1 Chemical and Product Use and Trends

Toluene is a high production volume chemical. Approximately 10 to 20 billion pounds per year of toluene are produced in the United States (U.S. EPA 2018), and it is also found naturally in crude oil and in the tolu tree (ATSDR 2017). It is a constituent of gasoline and is used to make many products, including nail products (ATSDR 2017) such as nail coatings and nail polish thinners (FDA 2017). Toluene is used as a solvent in nail polish to suspend the color, to form a smooth finish across the nail, and to evenly adhere polish to nails (ATSDR 2017; Zhou et al. 2016). Toluene-based thinners are sometimes added to nail polish and other coatings to increase fluidity (DTSC 2012). Toluene is reported as an ingredient in more than 40 nail coatings and one nail polish thinner in the California Safe Cosmetics Program Product Database (CDPH 2017). Environmental Working Group’s (EWG) Skin Deep cosmetics database includes five nail products, including nail coatings and thinners, that contain toluene (EWG 2017). Mintel’s Global New Products Database identifies 43 toluene-containing nail coating products introduced to the U.S. retail market, and 930 worldwide, since 2006 (Mintel 2018).

Analytical testing data confirms the use of toluene in nail products. Zhou et al. (2016) detected toluene in 26 out of 34 nail products analyzed, including base coat, top coat, nail polish thinner, gels, remover, and nail polish products, with concentrations ranging from 1.36 to 173,000 ppm ($\mu\text{g/g}$ by weight) (up to 17.3 percent). DTSC found comparable concentrations in its own testing of nail products in 2012. In that study, 10 of 12 nail coating products labeled “toluene-free” contained toluene at levels as high as 177,000 ppm (17.7 percent) (DTSC 2012). Further, eight of 13 nail coating products that made no claims to be toluene-free contained toluene at levels ranging from 110 to 120,000 ppm (0.011 percent to 12 percent) (DTSC 2012).

Use of nail products containing toluene in salons and at home has the potential to expose nail technicians and other salon workers, nail salon patrons, and nail product consumers to toluene. Nail technicians who work with toluene-containing products may experience daily chemical exposures, which can be exacerbated by their longer workdays and workweeks compared to employees in other sectors (Nails Magazine 2016; Quach et al. 2008). In California, there are more than 9,000 nail salons (Nails Magazine 2017) with 130,336 licensed manicurists (DCA 2017) and 314,552 cosmetologists (DCA 2018), many of whom use toluene-containing products. Toluene exposure is not just a concern for nail industry workers and their customers. Retail stores sell millions of nail products to consumers annually (Drug Store News 2016), and consumers are potentially exposed to toluene when they apply and remove toluene-containing nail products.

Nail technicians who work with toluene-containing products may experience daily chemical exposures, which can be exacerbated by their long workdays and workweeks.

In California, chemical exposure of nail industry workers is an environmental justice issue,⁶ as a large majority of nail industry workers are people of color and lower socioeconomic status (Quach et al. 2008). Approximately 59 to 80 percent of California nail salon workers are women of Vietnamese descent, many of whom face workplace safety challenges due to language barriers, limited education on chemical exposure from products, and limited availability and use of personal protective equipment (Quach et al. 2008; Quach et al. 2013). Clients receiving services in nail salons are exposed to harmful chemicals such as toluene on every visit (Ford 2014), and nail salon workers are potentially exposed to toluene daily.

⁶ California law defines environmental justice as “the fair treatment of people of all races, cultures, and incomes with respect to the development, adoption, implementation, and enforcement of environmental laws, regulations and policies” (Gov. Code, § 65040.12, subd. (e)).

2 POTENTIAL ADVERSE IMPACTS

This Section summarizes findings related to the potential adverse impacts of the Candidate Chemical as described in the SCP regulations. The emphasis of the adverse impact factors is to characterize the Candidate Chemical's toxicity and physical properties, and its mobility in the environment. The findings for this Candidate Chemical relate to the potential for one or more exposures described in Section 3 to contribute to or cause significant or widespread adverse impacts. Further clarification of each adverse impact factor is included below.

2.1 Physicochemical Properties

Reference: CAL. CODE REGS. tit. 22, § 69503.3(a)(1)(D).

Physicochemical properties can be helpful in predicting a chemical's behavior. A chemical's behavior in humans, wildlife, ecosystems, and the environment may indicate potential adverse public health and environmental impacts.

Table 1. Physical and chemical properties of toluene (HSDB 2016)

Property	Value
Color	Colorless
Physical state	Liquid
Molecular weight	92.139 g/mol
Density at 20 °C	0.8623 g/cm ³
Melting point	-94.9 °C
Boiling point	110.6 °C
Vapor density	3.1 (air = 1)
Vapor pressure at 25 °C	28.4 mm Hg
Henry's law constant at 25 °C	6.64 x 10 ⁻³ atm·m ³ /mol
Corrosivity	Noncorrosive liquid
Odor	Sweet, pungent, benzene-like odor
Odor threshold in air	2.14 ppm (8 mg/m ³)
Water solubility at 25 °C	526 mg/L
Solubility	Soluble in ethanol, benzene, diethyl ether, acetone, chloroform, glacial acetic acid, and carbon disulfide
Log octanol-water partition coefficient (Log K _{ow})	2.73
Log organic carbon-water partition coefficient (Log K _{oc})	1.57 to 2.25
Autoignition temperature	480 °C (896 °F)
Flashpoint	4 °C (40 °F, closed cup)
Lower explosive limit (LEL)	1.27 % by volume in air
Upper explosive limit (UEL)	7 % by volume in air
Conversion factor ppm (v/v) to mg/m ³ in air at 1 atm	1 ppm = 3.77 mg/m ³

2.2 Fate and Transport

2.2.1 Environmental fate

Reference: CAL. CODE REGS. tit. 22, § 69503.3(a)(1)(E).

Environmental fate describes a chemical's mobility in environmental media, transformation (physical, chemical, or biological), or accumulation in the environment or biota. A chemical's environmental fate in air, water, soil, and living organisms relates to its exposure potential hazard traits, as defined in the California Code of Regulations, Title 22, Chapter 54.

See Table 1 in Section 2.1 for physicochemical properties.

Nail product use or disposal is not expected to result in a significant release of toluene to soils or water. Toluene is a volatile chemical and is expected to partition into ambient air following its release to the environment. Toluene is not environmentally persistent and is rapidly degraded in soil, air, and water (ATSDR 2017; HSDB 2016).

Air

Based on an estimated vapor pressure of 28.4 mm Hg at 25 °C and as a function of toluene's physical properties, toluene readily volatilizes into the ambient atmosphere. Vapor-phase toluene degrades in the atmosphere by reacting with photochemically produced hydroxyl radicals with half-life estimates of 13 hours (ATSDR 2017; Howard 1991) or two days (HSDB 2016). Based on atmospheric conditions, the actual half-life may range from 10 to 104 hours (ATSDR 2017; Howard 1991). This hydroxyl radical degradation reaction forms cresol and benzaldehyde which break down further into basic hydrocarbons (Killus and Whitten 1982). Toluene is not expected to degrade by direct photolysis since it does not absorb light at wavelengths greater than 290 nm (HSDB 2016). Toluene is also oxidized by nitrogen dioxide, oxygen, and ozone in the atmosphere but at a much lower rate than by the hydroxyl radical reaction. Toluene oxidation by nitrogen dioxide, oxygen, and ozone can form benzyl nitrate and nitrotoluene (Atkinson 1990), and toluene photooxidation can form compounds such as carbonyl products (Cao and Jang 2008).

Soil

Toluene is expected to have high to moderate mobility in soil based on its K_{oc} values of 37 to 178 (HSDB 2016). Volatilization of toluene from moist soil surfaces is expected, given its Henry's Law constant of 6.64×10^{-3} atm·m³/mole, and toluene may volatilize from dry soil surfaces based on a vapor pressure of 28.4 mm Hg at 25 °C. With small releases of toluene, rapid volatilization is expected. For large releases, toluene's high soil mobility may result in migration to groundwater in addition to volatilization to air. Complete biodegradation of toluene in soil was observed in lab tests (HSDB 2016). The biodegradation half-life in various soils was reported as ranging from several hours to 71 days (HSDB 2016). These results suggest that biodegradation is an important environmental fate process in soil. Toluene is rapidly broken down in soils via oxidation processes under aerobic conditions and via nitrate or sulfate interactions under anaerobic conditions (ATSDR 2017).

Water

Toluene is moderately water soluble (526 mg/L) and rapidly degrades via oxidative metabolism under aerobic conditions in surface waters. It is also metabolized under anaerobic conditions through nitrate, sulfate, and phosphate interactions and microorganisms. Toluene's biodegradation half-life in groundwater is estimated to range from seven to 28 days (ATSDR 2017). Toluene rapidly volatilizes from surface water to air, with the volatilization rate dependent upon the water body and temperature conditions. The biodegradation half-life of toluene in surface waters is estimated to range from four to 22 days (ATSDR 2017).

At room temperature, toluene is a liquid volatile organic compound (VOC) as indicated by its Henry's law constant of $6.64 \times 10^{-3} \text{ atm}\cdot\text{m}^3/\text{mol}$. Toluene in nail products is expected to enter the environment primarily through evaporation into air and disposal into water via down-the-drain releases. Toluene may also be released to water in industrial effluents and by gasoline spills or leaks (ATSDR 2017).

A low log K_{ow} of 2.73 and measured bioconcentration factor of 8, 13, and 90 in herring, eels, and golden ide fish suggests toluene has a low likelihood to bioconcentrate in the fatty tissues of aquatic organisms (EC 2003; Franke et al. 1994).

2.2.2 Other harmful chemicals generated from the Candidate Chemical

Reference: CAL. CODE REGS. tit. 22, § 69503.3(a)(1)(G).

A Candidate Chemical may degrade, form reaction products, or metabolize into other chemicals that have one or more hazard traits. These metabolites, degradation products, and reaction products (which may or may not be Candidate Chemicals) may cause different adverse impacts from those of the parent chemical. In some cases, a Candidate Chemical's degradation or reaction products or metabolites may have the same hazard trait, and may be more potent or more environmentally persistent, or both, than the parent chemical. In such cases, adverse impacts may be more severe, or may continue long after, the Candidate Chemical's release to the environment.

Metabolism

In the human body, toluene is metabolized to the major metabolite hippuric acid and the minor metabolites ortho-cresol (o-cresol), meta-cresol (m-cresol), para-cresol (p-cresol), and benzaldehyde. Several of these metabolites are Candidate Chemicals for the Safer Consumer Products Program. DTSC lists ortho-, meta- and para-cresol as Candidate Chemicals (DTSC 2018), and CARB identifies ortho-, meta-, and para-cresol, as well as mixed cresols, as toxic air contaminants (CARB 2011). The U.S. EPA Integrated Risk Information System (IRIS) also lists o-cresol and m-cresol as neurotoxicants (U.S. EPA 2005a). DTSC also lists the family of cresols, or mixed cresols, as Candidate Chemicals (DTSC 2018), and ATSDR and OEHHA consider mixed cresols neurotoxicants (ATSDR 2011; OEHHA 2016).

Toluene is lipophilic and partitions into fatty tissues. The half-life in humans ranges from minutes to an hour based on the fat content of the compartment in the human body. Toluene distributes widely in the body and preferentially to the brain, liver, and kidney; it is capable of crossing the blood-brain barrier and the placenta, exposing the developing fetus to toluene (U.S. EPA 2005b). Most inhaled toluene is transformed and excreted in urine; however, a small amount is released unchanged in expired air (ATSDR 2017). In humans, toluene is

metabolized primarily by cytochrome p450 monooxygenases, alcohol dehydrogenases, and aldehyde dehydrogenases, which convert it to benzoic acid, which in turn binds with glycine and forms the primary urinary metabolite hippuric acid. However, a small amount of toluene may undergo aromatic ring oxidation to form the Candidate Chemicals o-cresol, m-cresol, and p-cresol (ATSDR 2017; IARC 1999; Pierce et al. 2002; WHO 2000).

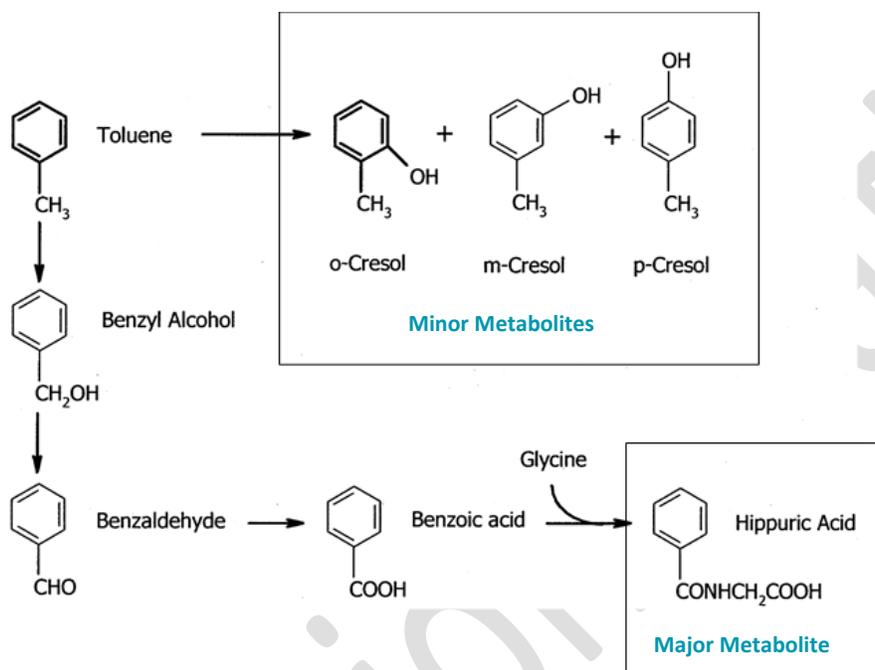


Figure 2. Pathways of toluene metabolism in humans (Pierce et al. 2002)

2.2.3 Behavior of the Candidate Chemical or its degradation products in the environment

Reference: CAL. CODE REGS. tit. 22, § 69503.3(b)(4)(H).

The Candidate Chemical and/or its degradation products can migrate into or distribute across different environmental media. These chemicals may persist or bioaccumulate in these environmental media or in biological tissues.

See Section 2.2.1 for additional information.

Toluene and its metabolites rapidly degrade across all environmental media and are not expected to accumulate in biological systems or persist in the environment. Volatilization to air is the predominant pathway for toluene release from the use and disposal of nail products (ATSDR 2017).

In 2010, CARB conducted a health risk assessment (HRA) of outdoor nail coating chemical emissions from nail salons. This HRA stated that outdoor air emissions from nail salons are not expected to have adverse health impacts to the public breathing the emissions outside of nail salons. This HRA focused on public health impacts from nail coatings emissions into outdoor air and did not evaluate the potential health impacts on nail salon workers from occupational chemical exposures (CARB 2010).

2.3 Hazard Traits and Environmental or Toxicological Endpoints

Reference: CAL. CODE REGS. tit. 22, § 69503.3(a)(1)(A).

The hazard traits and environmental or toxicological endpoints summarized in this Section are defined in the SCP regulations sections 69501.1(a)(36) and (33), respectively, both of which refer to OEHHA's Green Chemistry Hazard Trait regulations (California Code of Regulations, Title 22, Chapter 54).⁷ These include exposure potential, toxicological, and environmental hazard traits.

The hazard trait studies on toluene discussed below focus primarily on adverse impacts resulting from inhalation, since inhalation is the primary exposure route of nail industry workers and nail product consumers. However, exposure may also occur through dermal application of products and orally, from accidental ingestion and hand-to-mouth behavior.

Neurotoxicity (CAL. CODE REGS. tit. 22, § 69503.12)

The Agency for Toxic Substances Disease Registry (ATSDR), the U.S. EPA IRIS, the OEHHA Reference Exposure Level (REL) database, and the U.S. Centers for Disease Control and Prevention (CDC) Fourth National Report on Human Exposure to Environmental Chemicals all identify neurotoxicity as toluene's principal hazard trait (ATSDR 2017; CDC 2016; CDC 2017; OEHHA 2016; U.S. EPA 2005a). OEHHA has established a REL of 300 µg/m³ (80 ppb) for chronic exposure and 37,000 µg/m³ (9,800 ppb) for acute exposure (OEHHA 2016).

Toxic effects including dizziness, fatigue, headache, and decreased manual dexterity have been reported in workers exposed to toluene in various occupational settings. Individuals who use toluene to get intoxicated have suffered similar adverse effects (ATSDR 2017). Neurotoxicity from toluene exposure is well documented in humans as well as experimental animals (ATSDR 2017; U.S. EPA 2005a), and it is a significant hazard trait resulting from occupational inhalation exposure (U.S. EPA 2005a).

Neurotoxicity from toluene exposure is well documented in humans as well as experimental animals, and it is a significant hazard trait resulting from occupational inhalation exposure.

Most published human toluene exposure studies involve nervous system damage caused by toluene abuse or occupational exposure. Chronic degenerative brain disorder has been observed in toluene abusers. This disorder is characterized by damage to the white matter of the brain, which appears to become irreversible at some point following chronic inhalation exposure (Filley et al. 2004).

⁷<https://govt.westlaw.com/calregs/Browse/Home/California/CaliforniaCodeofRegulations?guid=I6E0E45C032A411E186A4EF11E7983D17&originationContext=documenttoc&transitionType=Default&contextData=%28sc.Default%29&bhcp=1>

Occupational studies of toluene exposure include:

- Rotogravure printing⁸ workers who were chronically occupationally exposed to mean toluene levels of 43 and 157 mg/m³ (11 and 42 ppm) reported symptoms including fatigue (60 percent), recent short-term memory problems (60 percent), concentration difficulties (40 percent), and mood changes (27 percent) (Ørbæk and Nise 1989).
- Another study demonstrated that rotogravure printing workers experienced a higher incidence of long-term auditory nervous system impacts compared to those in a group of workers of the same age but not professionally exposed to solvents (Abbate et al. 1993).
- Baelum et al. (1985) exposed two groups of subjects to 100 ppm (380 mg/m³) toluene for 6.5 hours; one group consisted of printing workers with long-term occupational solvent exposure, and the other group had no history of solvent exposure. Both groups experienced decreased manual dexterity, decreased color discrimination, and decreased accuracy in visual perception compared to controls. Impairment of color perception after acute toluene exposure had previously been seen only in people with a long-term history of solvent exposure (Baelum et al. 1985).
- A 1990 study of 30 female workers in an electronic assembly plant found that toluene exposure affected manual dexterity, verbal memory, and visual cognitive ability (Foo et al. 1990). Similar effects were found in a follow-up study (Boey et al. 1997).
- Echeverria et al. (1989) exposed a group of 42 paid college students to toluene for seven hours over three days at three different exposure levels of 0, 75, and 150 ppm (0, 280 and 560 mg/m³) and found that manual dexterity, verbal and visual short-term memory, and perception were affected in subjects with the highest toluene exposure level of 150 ppm (560 mg/m³). In this study, the incidence of headaches and eye irritations also increased with increasing dose levels (Echeverria et al. 1989).
- Eller et al. (1999) found that workers occupationally exposed to lower levels of toluene (greater than 100 ppm) for more than 12 years exhibited a range of self-reported neurological symptoms including concentration difficulties, impaired memory, and visual impairments.

Low-level toluene exposure in occupational settings may result in adverse outcomes:

- Kang et al. (2005) demonstrated that exposure to toluene in occupational settings at concentrations below 100 ppm is linked to neurobehavioral changes, and high-concentration toluene exposure could cause attention and concentration impacts as well as motor performance deficits.
- Chouaniere et al. (2002) conducted a cross-sectional study of workers at two printing plants who were exposed to very low levels of toluene (less than 40 ppm) and found associations between these exposures and reductions in memory test performances.

⁸ Rotogravure printing is a “system of printing based on the transfer of fluid ink from depressions in a printing plate to the paper. It is an intaglio process, so called because the design to be printed is etched or engraved below the surface of the printing plate. At the start of the gravure printing process, the plate is covered with ink and the surface is then wiped clean. When paper is pressed against the inked plate, the paper penetrates the sunken parts slightly and draws out the ink.” Encyclopædia Britannica (2017) Rotogravure printing. In. <https://www.britannica.com/technology/rotogravure-printing> Accessed March 2018

- Another researcher concluded that low-level exposure to neurotoxicants common to nail salons may result in mild cognitive and neurosensory changes similar to those observed among solvent-exposed workers in other settings (LoSasso et al. 2001; LoSasso et al. 2002).

Several animal studies illustrate neurotoxicity linked to toluene exposure:

- Toluene exposure via inhalation affects behavior, memory, and motor coordination (Forkman et al. 1991; von Euler et al. 1993).
- Oxidative stress in the brain may contribute to toluene-induced neurotoxic outcomes as demonstrated by Kodavanti et al. (2015), who conducted acute (six-hour) and subchronic studies (six hours per day, five days per week for 13 weeks) assessing the effects on rats exposed to toluene vapor on a variety of endpoints of oxidative stress. Their results showed that subchronic exposure affected oxidative stress parameters more than the acute exposures did (Kodavanti et al. 2015).
- Hillefors-Berglund et al. (1995) demonstrated increased dopamine binding (i.e., altered neurotransmitters)⁹ in rats' brains following chronic, low-dose (80 ppm and above) toluene inhalation exposure.
- Berenguer et al. (2003) also showed changes in neurotransmitter signaling following subchronic inhalation exposure of rats to 40 ppm toluene.
- A review by Win-Shwe and Fujimaki (2010) suggests that toluene, as shown in animal experiments, can adversely affect the hippocampus following acute and chronic inhalation exposure. The potential mechanisms involved in toluene toxicity in the brain may involve the dysregulation of the neurotransmitter glutamate, the excretion of proinflammatory proteins, and increased oxidative stress (Win-Shwe and Fujimaki 2010).
- A number of other animal studies have also shown neurotoxic effects in rats following acute toluene exposure (ATSDR 2017; Bowen and Balster 1998; Bushnell et al. 1985; Conti et al. 2012; Hogie et al. 2009; Huerta-Rivas et al. 2012; Kim et al. 1998; Kishi et al. 1988; López-Rubalcava et al. 2000; Mullin and Krivanek 1982; Páez-Martínez et al. 2008; Páez-Martínez et al. 2003; Taylor and Evans 1985; Tomaszycski et al. 2013; Wood and Colotla 1990; Wood et al. 1983).

Developmental Toxicity (CAL. CODE REGS. tit. 22, § 69402.3)

The California Proposition 65 list, the OEHHA REL database, and the CDC Fourth National Report on Human Exposure to Environmental Chemicals identify toluene as a developmental toxicant (CDC 2016; CDC 2017; OEHHA 1991; OEHHA 2016).

⁹ Neurotransmitters are chemical messengers released by neurons, also known as nerve cells, to stimulate neighboring neurons, muscles, and gland cells, allowing impulses to be passed from one cell to the next throughout the nervous system. Encyclopædia Britannica (2018) Neurotransmitter. In. <https://www.britannica.com/science/neurotransmitter> Accessed July 2018

Animal studies clearly implicate toluene as a developmental toxicant:

- A review by Donald et al. (1991) demonstrated in rats and mice that impaired fetal growth rate, following prenatal exposure to toluene, is the most consistently observed developmental endpoint in animal studies, as demonstrated by decreased pup weight and retarded skeletal development.
- One study found an association between maternal toluene exposure and decreased birth weight in rats, which persisted in male offspring into adulthood; maternal malnutrition increased fetal susceptibility to the effects of toluene, as indicated by effects on development of the skeleton (da Silva et al. 1990).
- Ungváry and Tátrai (1985) exposed mice to toluene via inhalation during pregnancy and saw decreased pup weight and abnormal skeleton development.
- In a separate study, fetuses of mice exposed to toluene via inhalation during pregnancy had additional or missing ribs (Courtney et al. 1986).
- In another study, high dose (2,000 ppm) maternal inhalation exposure of toluene caused weight suppression in mothers and offspring, high fetal mortality, and embryonic growth retardation in rats, but no fetal skeletal abnormalities were observed (Ono et al. 1995). However, skeletal abnormalities were observed when investigators attempted to mimic inhalation toluene abuse patterns in pregnant rats (Bowen et al. 2009).

In addition:

- Bowen and Hannigan (2013) found that rat pups that had been exposed, *in utero*, to toluene via inhalation experienced a reduction in postnatal growth.
- Roberts et al. (2003) and Roberts et al. (2007) observed that exposure of pregnant rats to toluene via inhalation resulted in maternal and developmental adverse outcomes, including lower than average pup birth weight and skeletal anomalies.
- Soberanes-Chávez et al. (2013) showed that exposure to toluene combined with stress during pregnancy resulted in lowered body weight gain in both mothers and offspring, as well as endocrine effects in mothers and decreased offspring food intake during the first weeks of life.

Toluene exposure during pregnancy is associated with a greater risk of delivering low body weight offspring.

A review and comparison of multiple animal studies demonstrated that increasing toluene exposure during pregnancy is associated with a greater risk of delivering low body weight offspring. Dose, administration route, animal weighing date, and animal model used all affected this association (Callan et al. 2016).

Expectant mothers who inhale toluene as a drug of abuse have given birth to infants with physical and developmental defects similar to fetal alcohol syndrome (Hannigan and Bowen 2010). These include mental deficiencies, facial malformations, abnormally small head size, and deformities in the fingertips (Arnold et al. 1994; Arnold and Wilkins-Haug 1990; ATSDR 2017; Erramouspe et al. 1996; Goodwin 1988; Hersh 1989; Hersh et al. 1985; Lindemann 1991; Pearson et al. 1994; Wilkins-Haug and Gabow 1991).

Cosmetologists are routinely exposed to a wide range of VOCs, including toluene, and studies illustrate some adverse pregnancy outcomes for cosmetologists compared to those of other working populations:

- Halliday-Bell et al. (2009) found that cosmetologists had a 50 percent higher risk than teachers of having babies who were small for their gestational age.
- Herdt-Losavio et al. (2009) compared pregnancy outcomes of 15,003 New York State licensed cosmetologists (hair and nail technicians), 4,246 licensed Realtors, and 12,171 mothers from the general population. They found an increased risk of low birth weight among newborns of cosmetologists compared with newborns of Realtors and newborns in the general population.
- In a study of 8,356 North Carolina cosmetologists, investigators found associations between spontaneous abortion and the number of hours worked per day in cosmetology, the number of chemical services performed per week, and work in salons where nail sculpturing was performed by other employees (John et al. 1994).

The effects reported in these studies were not attributed to toluene exposure alone. However, it is noteworthy that developmental toxicity was observed, given that toluene is a developmental toxicant present in some nail products.

Neurodevelopmental Toxicity (CAL. CODE REGS. tit. 22, § 69403.11)

While decreased body weight is toluene's most consistently observed developmental endpoint, there is also evidence that toluene exposure may result in neurodevelopmental toxicity (Grandjean and Landrigan 2006):

- Laslo-Baker et al. (2004) showed that *in utero* exposure to organic solvents in the workplace is associated with impacts to cognitive function, language, and behavior.
- Hass et al. concluded that inhalation exposure to toluene during brain development resulted in prolonged neurodevelopmental toxicity in rats, as evidenced by increased motor activity in both sexes and impaired cognitive function in female offspring (Hass et al. 1999).
- Hougaard et al. (1999) showed effects on cognitive function among pups of rats exposed *in utero* to toluene. These effects on cognitive function were most pronounced in female offspring (Hougaard et al. 1999).
- Samuel-Herter et al. (2014) found age-dependent neurobiological effects when rats, ranging from adolescence to adulthood, were exposed to toluene via inhalation. The age of the rats at the time of exposure affected the time of recovery of motor functions resulting from intoxication.
- Chen et al. (2011) demonstrated that exposing rats to toluene during brain growth spurt and adolescence resulted in signaling biochemical changes in the hippocampus, which in turn could lead to neurobehavioral disturbances. This is notable since the hippocampus is responsible for memory and learning processes in the developing brain (Bauer and Pathman 2008).
- Interestingly, Win-Shwe et al. (2012) found that the pups of mice exposed to low levels of toluene (5 or 50 ppm) in air while pregnant exhibited increases of neuroinflammatory gene expression relative to controls. Changes in gene expression may indicate the potential for later changes in related proteins and toxic outcomes.

Respiratory Toxicity (CAL. CODE REGS. tit. 22, § 69403.1)

The OEHHA REL database and the CDC Fourth National Report on Human Exposure to Environmental Chemicals identify toluene as a respiratory toxicant (CDC 2016; CDC 2017; OEHHA 2016).

Several studies report respiratory tract irritation due to intentional or accidental toluene exposure via inhalation.

- Deschamps et al. (2001) reported mucous membrane irritation in workers chronically exposed to toluene. Controlled studies of human exposure to toluene have shown similar results (Ørbæk et al. 1998; Österberg et al. 2003).
- Echeverria et al. (1989) and Andersen et al. (1983) reported nasal irritation in humans after acute exposure to airborne toluene at concentrations of 100 ppm (376.85 mg/m³).
- Experimental animal studies also documented nasal irritation (ATSDR 2017). Specifically, the National Toxicology Program (NTP) study demonstrated that inhalation exposure of both mice and rats to toluene resulted in deterioration of the olfactory¹⁰ and respiratory epithelium¹¹ and inflammation of the lining of the nasal cavity (NTP 1990).
- Further, chronic toluene abuse in humans is associated with lung damage and emphysema (Schikler et al. 1984).

One study of nail technicians demonstrated a higher prevalence of reported upper and lower respiratory symptoms in comparison to nonexposed controls; however, the cause or causes of the symptoms cannot be determined from this study design, as no clinical assessment was carried out (Harris-Roberts et al. 2011).

Nephrotoxicity (CAL. CODE REGS. tit. 22, § 69403.10)

The U.S. EPA IRIS identifies the kidney as a critical noncancer target following chronic oral exposure (U.S. EPA 2005a). NTP demonstrated increased kidney weight in mice and rats following oral exposure to toluene (NTP 1990). Numerous studies in humans support this finding; they document kidney damage after deliberate, acute inhalation exposure to toluene (Bonzel et al. 1987; Bosch et al. 1988; Caravati and Bjerk 1997; Fischman and Oster 1979; Kamijima et al. 1994; Kroeger et al. 1980; O'Brien et al. 1971; Streicher et al. 1981; Taher et al. 1974; U.S. EPA 2005b). Abuse of toluene is associated with metabolic acidosis (i.e., acid accumulation in the body), hyperchloremia (i.e., abnormally high blood chloride levels), and hypokalemia (i.e., abnormally low blood potassium levels) – all signs of kidney damage (Batlle et al. 1988).

Dermatotoxicity (CAL. CODE REGS. tit. 22, § sections 69403.2)

Toluene is absorbed through skin (Aitio et al. 1984; ATSDR 2017; Boman et al. 1995; Brown et al. 1984; Dutkiewicz and Tyras 1968; Sato and Nakajima 1978; Weschler and Nazaroff 2014), and solvents may enhance the penetration of other chemicals through the skin (Andersen et al. 2014). Dermal toluene exposure can cause skin irritation in humans, possibly due to its propensity to remove protective skin oils (ATSDR 2017). Dermal

¹⁰ The olfactory epithelium is specialized epithelial tissue inside the nasal cavity that is involved in smell.

¹¹ Respiratory epithelium is a type of ciliated epithelial tissue which lines most of the respiratory tract, where it serves to moisten and protect the airways.

exposure studies in guinea pigs, mice, and rabbits suggest that undiluted toluene is slightly to moderately irritating to the skin (Anderson et al. 1986; ATSDR 2017; Kronevi et al. 1979; Saito et al. 2011; Wolf et al. 1956).

Immunotoxicity (CAL. CODE REGS. tit. 22, § 69403.8)

The State Water Resources Control Board (SWRCB) established a Maximum Contaminant Level (MCL) for toluene in drinking water based on its immunotoxicity (OEHHA 1999; SWRCB 2014). Hsieh et al. showed a variety of immunotoxic effects including decreased thymus weight¹² and dose-dependent effects on suppression of antibody response. However, more studies are needed to confirm these effects (Hsieh et al. 1990; Hsieh et al. 1989; Hsieh et al. 1991).

Cardiovascular Toxicity (CAL. CODE REGS. tit. 22, § 69403.1)

Cardiac arrhythmia (i.e., irregular heart rate), tachycardia (i.e., fast heart rate), and bradycardia (i.e., slow heart rate) have all been reported in humans following acute toluene inhalation exposure (Anderson et al. 1982; ATSDR 2017; Camara-Lemarroy et al. 2015; Einav et al. 1997; Meulenbelt et al. 1990; Shibata et al. 1994; Vural and Ogel 2006). Death due to cardiac arrhythmia following intentional toluene inhalation has also been reported (ATSDR 2017). Of interest, animal studies with high-dose inhalation of toluene showed no impacts to the cardiovascular system (NTP 1990), and other laboratory animal studies do not provide convincing support for cardiovascular toxicity following toluene inhalation exposure (ATSDR 2017; Bruckner and Peterson 1981; CIIT 1980; NTP 1990). Some individuals may be more susceptible than others to potentially fatal arrhythmias due to differences between people in cardiac response to toluene (ATSDR 2017).

Hepatotoxicity (CAL. CODE REGS. tit. 22, § 69403.7)

SWRCB established an MCL for toluene in drinking water based on its hepatotoxicity (OEHHA 1999; SWRCB 2014). However, studies focused on chronic toluene abusers or occupationally exposed humans present conflicting findings on the potential liver impacts of toluene exposure. Animal studies have yielded similarly inconsistent results (ATSDR 2017; Dick et al. 2014; Gotohda et al. 2009; Meulenbelt et al. 1990; Tähti et al. 1983; Ungváry et al. 1982; Wang et al. 1996).

Ocular Toxicity (CAL. CODE REGS. tit. 22, § 69403.13)

The CDC Fourth National Report on Human Exposure to Environmental Chemicals identifies ocular toxicity as a hazard trait following toluene exposure (CDC 2016; CDC 2017). Kiyokawa et al. (1999) reported that a group of 15 patients had severe vision effects, specifically optic nerve damage, after prolonged toluene abuse. Two independent studies evaluated the effects of occupational toluene vapor exposure on color perception and demonstrated a significant impairment compared to controls (Muttray et al. 1999; Zavalic et al. 1998). Further, Echeverria et al. (1989) observed that eye irritations increased with increasing dose levels of toluene in a group of 42 paid college students exposed to toluene for seven hours over three days at three different exposure levels (0, 75, and 150 ppm or 0, 280 and 560 mg/m³).

¹² Lower weight of the thymus, a specialized organ of the immune system, signifies potential adverse impact to the immune system.

Ototoxicity (CAL. CODE REGS. tit. 22, § 69403.14)

The CDC Fourth National Report on Human Exposure to Environmental Chemicals identifies ototoxicity as a hazard trait following toluene exposure (CDC 2016; CDC 2017). McWilliams et al. (2000) demonstrated that toluene exposure for up to four weeks in guinea pigs resulted in reversible hearing loss, while Pryor et al. (1984) demonstrated that toluene-induced hearing loss in male rats persisted over a three-month period.

2.4 Related Chemicals and Their Adverse Impacts

2.4.1 Cumulative effects with other chemicals

Reference: CAL. CODE REGS. tit. 22, § 69503.3(a)(1)(C).

Cumulative effects occur from cumulative exposures to the Candidate Chemical and other chemicals with similar hazard traits or endpoints.

Nail salon workers are chronically exposed to several different chemicals simultaneously. In a study of California nail salons, the average measured work-shift total VOC concentrations of toluene, ethyl acetate, and isopropyl acetate in indoor air ranged from 3 to 25 mg/m³ (0.80 to 6.6 ppm), which is much higher than the World Health Organization (WHO) recommended guideline of 0.26 mg/m³ (0.069 ppm) for toluene in indoor air (Quach et al. 2011; WHO 2000). Nail salon workers reported health problems including headaches and eye, nose, and throat irritation (Quach et al. 2011). In another study, Nguyen (2016) measured indoor air VOC concentrations at eight Los Angeles nail salons, reporting average concentrations of acetone, isopropyl alcohol (IPA), and methyl methacrylate (MMA) as much as six times higher than those measured in other nail salon indoor air quality studies in Alameda County, California, by Quach (Quach et al. 2011) and Salt Lake City, Utah (Alaves et al. 2013).

Some studies indicate potential interactions between toluene and other chemicals may adversely impact metabolism, chemical excretion, and resulting toxicity. Simultaneous metabolism of toluene and xylene was reduced after co-exposure to high concentrations of both chemicals (ATSDR 2017; Tardif et al. 1991; Tardif et al. 1992). Similarly, while co-exposure of toluene, methyl ethyl ketone (MEK), and IPA at low concentrations in rats had no effect on the urinary excretion of the toluene metabolite hippuric acid, co-exposure to concentrations of MEK and IPA that were more than twice that of toluene resulted in reduced toluene metabolite levels in urine (ATSDR 2017; Uaki et al. 1995). This may be relevant to nail salons due to the presence of MEK, isopropyl alcohol, and toluene in various nail products. In fact, MEK, IPA, and toluene were all detected in nail salons in the greater Los Angeles area (Nguyen 2016). These studies indicate the potential for toluene and other volatile organic solvents to operate under similar mechanisms of metabolism. In general, metabolic pathways for high doses of toluene, MEK, and IPA appear similar, and co-exposure to these chemicals from nail products may result in decreased chemical excretion from the body and increased adverse effects. However, it is unknown at what levels mixed chemical exposure could alter human metabolism and excretion of these chemicals. More studies are needed to understand these interactions and their role in contributing to adverse impacts.

2.4.2 Structurally or mechanistically similar chemicals

Reference: CAL. CODE REGS. tit. 22, § 69503.3(a)(3).

Some chemicals may lack sufficient data to definitively establish presence or absence of harm. In such cases, DTSC may also consider data from other chemicals closely related structurally to the Candidate Chemical to identify potential public health and environmental impacts.

DTSC is not basing its proposal on this factor.

2.5 Populations That May Be Harmed by the Candidate Chemical

2.5.1 Human populations and nonhuman organisms that may experience adverse impacts from exposure to the Candidate Chemical

Reference: CAL. CODE REGS. tit. 22, § 69503.3(a)(1)(F).

This Section identifies specific populations of humans and environmental organisms that may be harmed if exposed to the Candidate Chemical, based on the hazard traits identified in Section 2.3 and the type of exposures (e.g., single, intermittent, or chronic).

See Section 2.3, Section 2.4, Section 2.5, Section 3.2, and Section 3.3 for additional information.

Toluene has the potential to contribute to or cause adverse impacts to humans, especially chronically exposed populations such as nail industry workers, and sensitive subpopulations such as pregnant women, fetuses, infants, children, and adolescents.

Nail salon customers, nail product consumers, and their infants and children may potentially be exposed to toluene from nail products. Nail salon customers and nail product consumers may experience inhalation, dermal, or oral toluene exposure. Patrons and consumers generally experience less frequent, shorter-duration toluene exposures than nail salon workers and, consequently, their likelihood of experiencing adverse impacts from toluene exposure from nail products is correspondingly lower. Infants and children who accompany their parents to work at nail salons or use nail products themselves may also be exposed to toluene in nail products.

2.5.2 Sensitive subpopulations, species, or environments that have the potential for adverse impacts from exposure to the Candidate Chemical

Reference: CAL. CODE REGS. tit. 22, §§ 69503.3(a)(1)(F) and 69503.3(a)(2).

Sensitive subpopulations, environmentally sensitive habitats, endangered and threatened species, and impaired environments have special consideration as they may be more vulnerable than the general population.

Sensitive subpopulations that may be impacted by exposure to toluene from nail products include nail industry workers, pregnant women (including their fetuses), infants, children, and adolescents.

Nail industry workers may be impacted by exposure to toluene due to its frequent use in the workplace and some nail technicians work while pregnant; thus, their fetuses are also at risk of toluene exposure. Nail salon

workers may have daily exposure to toluene. They often have longer workdays and workweeks compared to employees in other sectors (Quach et al. 2008). California's nail industry work force is composed of approximately 130,000 licensed nail technicians (DCA 2017). According to the U.S. Census Bureau, 90 percent of all nail salons in California are minority-owned, and 68 percent of salons are Vietnamese-owned (U.S. Census Bureau 2012). Reportedly, 97 percent of U.S. nail technicians are female and many are of childbearing age (Nails Magazine 2017). Pregnant women and their fetuses may be at greater risk of adverse impacts from toluene exposure (Quach et al. 2008; Quach et al. 2013). (See Section 2.3 of this document for studies describing toluene-related developmental toxicity.)

Studies indicate that nail salon workers may suffer from a higher incidence of certain health problems than the general population. For instance, a 2008 study examined self-reported health effects of nail salon workers participating in a community outreach program. The nail salon workers surveyed were predominantly Vietnamese, female, and generally worked long hours. Health effects reported included musculoskeletal disorders, respiratory symptoms, skin problems, and headaches (Roelofs et al. 2008). In addition to a higher incidence of specific health problems, a recent study suggests that nail care technicians experience a faster deterioration of their overall health compared to controls as a result of chronic exposure to low levels of VOCs (Grešner et al. 2017).

Studies indicate that nail salon workers may suffer from a higher incidence of certain health problems than the general population.

In California, chemical exposure of nail industry workers is an environmental justice issue, as a large majority of these workers are people of color and of lower socioeconomic status. It is estimated that 59 to 80 percent of nail salon workers in California are women of Vietnamese descent (Quach et al. 2008). Many of these workers face workplace safety challenges due to language barriers, limited education on chemical exposure from products, and limited availability and use of personal protective equipment (Quach et al. 2008; Quach et al. 2013). In addition, evidence suggests that some Asian populations may be genetically sensitive to toluene due to a defective gene for the aldehyde dehydrogenase enzyme, which leads to a decreased rate of toluene metabolism (Greenberg 1997).

Infants and children are especially vulnerable to toluene exposure from nail products if they accompany their parents to work at a nail salon or are nail salon customers. They are a sensitive subpopulation because of their increased ingestion and inhalation rates per unit of body weight, rapid development, immature physiological ability to detoxify environmental contaminants, and behavioral characteristics that predispose them to increased exposures to environmental contaminants (U.S. EPA 2011). Further, studies demonstrate that infants and children have differences in metabolic enzyme levels, including differences in several phase II detoxification enzymes, compared to adults (Leeder and Kearns 1997; Nakajima et al. 1992; Vieira et al. 1996). Other studies show that infants and children have higher brain mass per unit of body weight, higher cerebral blood flow per unit of brain weight, and higher breathing rates per unit of body weight than adults (Miller et al. 2002). These differences result in greater sensitivity to infants and children and increased likelihood or severity of adverse impacts.

Nail salon customers, who may include pregnant women and children, may be exposed to toluene both at nail salons and at home. In a 2010 personal-care product-use survey of 604 households in Northern and Central

California, Wu et al. (2010) found that 45 percent of girls younger than 5 years old use nail polish, and this increased to 79 percent for girls over 5. This study showed a correlation between nail product use by parents and children in the same household, suggesting that either parents use nail products on their children or that parental use patterns influence those of their children, resulting in exposure to chemicals in the products (Wu et al. 2010).

3 FACTORS RELATED TO POTENTIAL EXPOSURE TO THE CANDIDATE CHEMICAL IN THE PRIORITY PRODUCT

This Section summarizes significant findings related to the exposure factors that are relevant to this product-chemical combination because they may contribute to or cause significant or widespread adverse impacts. Further clarification of each exposure factor is included below.

3.1 Presence and Use Patterns of the Product

3.1.1 Market presence of the product

Reference: CAL. CODE REGS. tit. 22, §§ 69503.3(b)(1)(A) and (B).

Product market presence information may be used as a surrogate to assess potential exposures to the Candidate Chemical in the product. This information may include statewide sales by volume, the number of units sold or amount of sales generated, or information on the targeted customer base.

Toluene, formaldehyde, and DBP have been historically called the “toxic trio” when used together in nail products. While nail product manufacturers have largely phased out the use of formaldehyde and DBP, multiple nail products still contain toluene. These include nail polishes and other coatings, nail hardeners, nail polish thinner, and polish removers (CDPH 2017; EWG 2017; FDA 2017; Mintel 2018). Zhou et al. detected toluene in 26 out of 34 nail products analyzed, including base coat, top coat, nail polish thinner, gels, remover, and nail polish products. Environmental Working Group’s (EWG) Skin Deep cosmetics database lists five nail products, including coatings and thinner, containing toluene as an ingredient (EWG 2017). Toluene is reported as an ingredient in more than 40 nail coatings and one nail polish thinner in the California Safe Cosmetics Program Product Database (CDPH 2017). Mintel’s Global New Products Database identifies 43 toluene-containing nail coating products introduced to the U.S. retail market, and 930 worldwide, since 2006 (Mintel 2018). Mintel and EWG’s databases include only retail nail products (not intended for professional use); Mintel’s data is limited to products under \$25. Therefore, there may be a greater number of toluene-containing nail products available for sale or purchase in California.

U.S. Census data and Simmons National Consumer Survey data calculated by Statista showed that 105.41 million women in the United States used nail polish or other nail products in 2017 (Statista 2017a), and this figure is projected to increase to 122.65 million in 2020 (Statista 2017b). Annual sales of various nail products from U.S. retail outlets exceed \$1 billion per year (Drug Store News 2016). From June 2015 to May 2016, nail polish sales exceeded \$741 million (or 204 million products sold) at chain drug stores, supermarkets, discount stores, and club and dollar stores (Drug Store News 2016).

Rapid increase in the number of nail salons, recent revenue figures, the number of nail salon workers, and the types of services they provide all illustrate the potential for exposure to toluene and other chemicals from professional nail products and services. In 2016, \$8.53 billion was spent on nail services in the United States (Nails Magazine 2017). In California alone, there are more than 9,000 nail salons (Nails Magazine 2017) with 130,336 licensed manicurists (DCA 2017) and an additional 314,552 licensed cosmetologists (DCA 2018). According to one survey, 95 percent of U.S. nail technicians offer nail polish services, 67 percent offer UV gels, 84 percent offer acrylics, and 82 percent offer nail art (Nails Magazine 2015).

Toluene exposure is not just a concern for nail industry workers and their customers. Retail stores sell millions of nail products to consumers annually (Drug Store News 2016), and consumers are potentially exposed to toluene when they apply and remove toluene-containing nail products. Acrylic nail products, nail polishes, and gel nail products that contain toluene are sold in retail stores and local beauty supply stores (EWG 2017; SF Environment 2017).

UV gels and gel polishes are among the nail products that may contain toluene. UV gels (also known as gel nails) have become a popular product at nail salons. UV gels are more durable than traditional nail polish and are easier to apply and remove compared to acrylics. As stated above, roughly 67 percent of nail technicians offer UV gels at their salons (Nails Magazine 2015). Gel polish is also a popular option for at-home use. Gel polish has the look, feel, and long-lasting quality of traditional UV and LED gels but does not require a UV or LED light to dry. Ten percent of women who apply nail polish at home report that they use gel polish (Romanowski 2015). U.S. at-home gel polish sales revenue in 2012 totaled \$25 million and is expected to grow in subsequent years (Brookman 2013).

\$8.53 billion
was spent on nail
services in the United
States in 2016.

3.1.2 Intended use of the product

Reference: CAL. CODE REGS. tit. 22, §§ 69503.3(b)(1)(C) and 69503.3(b)(4)(D)1.

Potential exposures can also be inferred by assessing how a product is typically used, the typical useful life (i.e., replacement frequency) of durable products, the typical rate of consumption of consumable products, the frequency of use, and the typical quantity consumed per use. The SCP regulations give special consideration to household and recreational use.

See Section 1.2, Section 1.3, and Section 3.1.1 for additional information.

Use of nail products containing toluene in salons and at home has the potential to expose nail technicians and other salon workers, nail salon patrons, and nail product consumers to toluene. Nail technicians who work with toluene-containing products may experience daily chemical exposures, which can be exacerbated by their longer workdays and workweeks compared to employees in other sectors (Nails Magazine 2016; Quach et al. 2008).

The frequency of consumer nail polish application and removal varies, but it is common for some nail salon customers to get a professional manicure every one to two weeks and to self-apply a top coat every two to three days (Sally Beauty Supply 2017). The frequency of other nail product services also varies.

In a 2010 study, data on use patterns of 30 personal care product types were collected from 604 households in Northern and Central California. Nail polish use frequency data was collected for female participants from various age groups. Female participants in this study included children, their mothers, and adults who were 55 years old or older in 2010. The frequency of professionally applied and self-applied nail polish uses for adult females and child participants are shown in

Table 2 (Wu et al. 2010).

Table 2. Nail polish use frequency per month for female participants in California in 2010 (Wu et al. 2010)

Participant Type and Age (in years)	Number of Participants	Nail Polish (Self) User %	Nail Polish (Professional) User %
Adult < 55*	374	53	81
Adult > 55	99	39	77
Child < 5	185	45	---
Child > 5	31	79	---

*All participants under 55 years of age had young children at home.

**Participants older than 16 years old are considered as adults in this study.

***In this study, the mothers with less than 12 years of education were oversampled to counter the well-known low rates of participation in research for this socio-demographic group.

The majority of adult female participants in the study, in both age groups, received professional nail services more frequently than they self-applied nail polish; professional nail polish use frequency for females with young children was 81 percent (Table 2) (Wu et al. 2010). A greater proportion of college-educated women used professional nail services than non-college-educated women (Wu et al. 2010). Nail polish use was common among even the youngest study participants: 45 percent of girls age 5 and under and 79 percent of girls over 5 used nail polish (Table 2) (Wu et al. 2010). This study showed a correlation between use of nail products among parents and children in the same household, suggesting that either parents use nail products on their children in similar patterns as they use them on themselves or that parental use patterns influence their children's use of nail products and, thus, their exposure to chemicals from the products (Wu et al. 2010).

3.1.3 Household and workplace presence of the product and other products containing the Candidate Chemical, and aggregate effects

Reference: CAL. CODE REGS. tit. 22, §§ 69503.3(a)(1)(B) and 69503.3(b)(3).

The potential for exposure to the Candidate Chemical in the product relates to how common the product is in households and workplaces. The household and workplace presence of other products that contain the same Candidate Chemical may increase the potential for aggregate effects.

In addition to use in nail products, toluene is added to gasoline and is used in the manufacture of many products including paint thinners, adhesives, paints, inks, varnishes, glues, cleaning solutions, shoe and nail polishes, carpets, vinyl flooring, wood boards, rubber and dyes (ATSDR 2017). The U.S. Department of Health and Human

Services' Household Products Database lists multiple toluene-containing products that may be used inside the home, including various home maintenance products, arts and crafts products, auto products, paints, and pet care products (HHS 2017). Tobacco smoke can also be a source of indoor toluene exposure (ATSDR 2017).

Nail technicians who use multiple toluene-containing nail products in a workday may experience aggregate exposure to the Candidate Chemical. Toluene is found in several different products within a nail salon (including nail polish and other coatings and nail polish thinner) (CDPH 2017; EWG 2017; FDA 2017; Mintel 2018; Zhou et al. 2016). As noted previously, Zhou et al. (2016) detected toluene in 26 different nail products, including base coat, top coat, nail polish thinner, gels, remover, and nail polish products, with concentrations ranging from 1.36 to 173,000 ppm ($\mu\text{g/g}$ by weight) (up to 17.3 percent toluene content). In a study conducted by DTSC, 10 of 12 nail coating products labeled "toluene-free" contained toluene levels as high as 177,000 ppm (17.7 percent) (DTSC 2012). Further, eight of 13 nail coating products which made no claims to be toluene-free contained toluene, at levels ranging from 110 to 120,000 ppm (0.011 percent to 12 percent) (DTSC 2012).

The primary source of toluene in outdoor air is from automobile exhaust (ATSDR 2017). Outdoor air contaminated with toluene can migrate into indoor air environments such as homes and workplaces and potentially contribute to aggregate exposure.

Levels of toluene measured in ambient rural air, ambient urban air, and indoor air are an average of 1.3, 10.8, and $31.5 \mu\text{g}/\text{m}^3$ (0.34, 2.9, and 8.4 ppb), respectively (U.S. EPA 2012). Urban air has higher toluene concentrations compared to rural air, which is likely due to automobile emissions. It is significant that indoor air has the highest detected toluene levels, suggesting additional sources inside buildings.

While toluene is found in multiple products and is detected in indoor air, DTSC is unable to adequately assess aggregate exposure from all these sources or how these exposures compare with toluene exposure from nail products. Nevertheless, toluene exposure by itself is of concern to nail salon workers' health regardless of potential aggregate exposure.

3.2 Potentially Exposed Populations and Product-Use Scenarios

3.2.1 Targeted customer base

Reference: CAL. CODE REGS. tit. 22, § 69503.3(b)(1).

This Section may include information on who typically buys or uses the product, and where the product is marketed or sold.

Most nail product purchasers and users in the United States are female. They come from various age groups and many belong to sensitive subpopulations such as nail industry workers, infants, children, adolescents, and pregnant women (Pak et al. 2013; Wu et al. 2010). U.S. nail industry workers are mostly low-income, women of color, and non-native English speaking women of childbearing age (Nails Magazine 2017).

Nationwide, there are approximately 69,738 nail salons with 393,581 licensed manicurists (Nails Magazine 2017); in California alone, there are more than 9,000 nail salons (Nails Magazine 2017) with 130,336 licensed manicurists (DCA 2017) and 314,552 cosmetologists (DCA 2018). Quach et al. (2008) estimate that 59 to 80

percent of nail technicians in California are of Vietnamese descent. According to the U.S. Census Bureau, 90 percent of all nail salons in California are minority-owned, and 68 percent are Vietnamese-owned (U.S. Census Bureau 2012). Reportedly, 97 percent of nail technicians are female, 64 percent are nonwhite, 56 percent are Vietnamese, and many are of childbearing age (Nails Magazine 2017; Pak et al. 2013). Nail technicians can be found in a variety of different types of salons including nail salons, full-service salons offering nail services, mobile or home-based salons, and spas (Nails Magazine 2017).

According to one survey, 97 percent of nail salon customers are female (Nails Magazine 2017). More than 60 percent of female nail salon customers are of childbearing age (Figure 3).

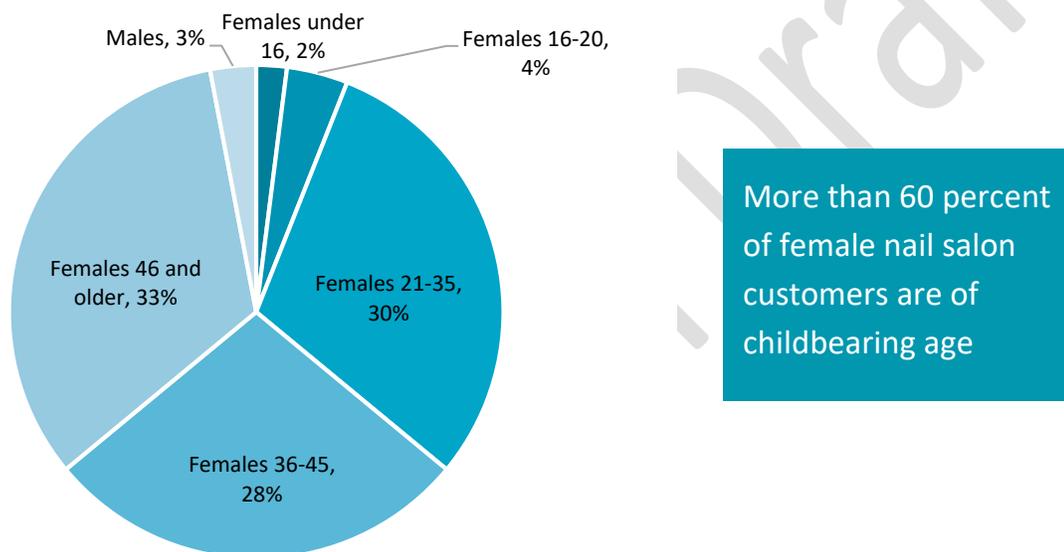


Figure 3. Demographic makeup of nail salon customers (Nails Magazine 2017)

3.2.2 Use scenarios that may contribute to adverse impacts

Reference: CAL. CODE REGS. tit. 22, § 69503.3(b)(4)(D).

The SCP regulations consider a variety of uses that may contribute to the exposure to the product-chemical combination. These include household and recreational use, use by sensitive subpopulations, and use by workers, customers, clients, and members of the general public in homes, schools, workplaces, or other locations.

See Section 2.5, Section 3.1, Section 3.2.1, Section 3.3, and Section 3.5 for additional information.

Use of nail products containing toluene in salons and at home has the potential to expose nail technicians and other salon workers, nail salon patrons, and nail product consumers to toluene. Nail technicians who work with toluene-containing products experience potentially harmful daily chemical exposures, which can be exacerbated by their longer workdays and workweeks compared to employees in other sectors (Nails Magazine 2016; Quach et al. 2008).

Inhalation is an important exposure route for both nail salon workers and consumers who use toluene-containing products in salons and at home (Ford 2014). When nail products containing toluene are opened to allow for application, toluene volatilizes into the indoor air and is breathed in by nail technicians and their customers. Building parameters, air exchange rates, ventilation, weather conditions, seasonal variations (Grešner et al. 2016), and the use of personal protective equipment (OSHA 2017; Quach et al. 2012; Quach et al. 2013) all affect toluene exposure potential. Ventilation, in particular, is a critical factor in determining indoor air conditions and potential exposure to workers and consumers. While adequate ventilation reduces worker exposure, some salons don't have it (Goldin et al. 2014; NYSDOH 2016). Respiratory problems from chemical exposure are made worse by inadequate ventilation in salons (Marlow et al. 2012). Roelofs and Do (2012) showed that many salons in the Boston area did not have adequate ventilation.

The average nail salon is a single room with one to 10 workstations or tables (Yang and Han 2010) and is sometimes located in an enclosed building, such as an indoor mall (Quach et al. 2011). A nail technician sits on one side of a table facing a client on the other side. This proximity means that salon workers are using nail products close to their breathing zone, exposing themselves to the chemicals these products contain (Yang and Han 2010). Further, nail salons tend to be small work spaces (a mean area of 512 square feet in Alameda County, California) with inadequate ventilation, which increases the magnitude of potential inhalation exposure (Quach et al. 2011).

As noted previously, nail salon workers often work long hours and may be simultaneously exposed to multiple toluene-containing nail products. As mentioned in Section 3.1.2, the median nail technician works 36 or more hours per week and services 16 to 20 customers (Nails Magazine 2017). Ten percent of nail technicians service 36 or more customers per week (Nails Magazine 2017).

Home users of toluene-containing nail products are generally exposed to lower air concentrations of toluene than salon workers (U.S. EPA 2005b). However, in some cases home users' exposure may be greater (e.g., if a consumer uses nail products in a small space with little or no ventilation) (Kopelovich et al. 2015; Marlow et al. 2012). Curry et al. (1994) described a personal monitoring study of inhalation exposure to toluene during normal in-home consumer use of nail coating products at five different residences in California. Prior to the nail coating application, toluene was not detected in any of the air samples above the detection limits of 200 $\mu\text{g}/\text{m}^3$ (50 ppb) in air. However, the average toluene levels measured in air during nail coating application ranged from 3,200 to 9,200 $\mu\text{g}/\text{m}^3$ (850 ppb to 2,400 ppb), while the post-application concentrations ranged from 200 to 1,700 $\mu\text{g}/\text{m}^3$ (50 to 450 ppb) (Curry et al. 1994). Measured toluene levels during nail coating application exceeded the OEHHA established REL of 80 ppb (300 $\mu\text{g}/\text{m}^3$) for toluene in indoor air (OEHHA 2016).¹³ These levels are potentially harmful to human health.

¹³ The REL for toluene is set at a level which is established to protect humans from adverse impacts to the respiratory and nervous symptoms. OEHHA (2016) Acute, 8-hour and Chronic Reference Exposure. Office of Environmental Health Hazard Assessment (OEHHA). In. <http://www.dtsc.ca.gov/SCP/upload/2-E-CA-RELS.pdf> Accessed July, 2017

3.3 Exposures to the Candidate Chemical Throughout the Product Life Cycle

3.3.1 Indicators of potential exposures to the Candidate Chemical from the product

Reference: CAL. CODE REGS. tit. 22, § 69503.3(b)(2).

The SCP regulations consider various data that indicate potential for exposure to the Candidate Chemical or its degradation products, including: (i) the Candidate Chemical's presence in and release from the product; (ii) monitoring data indicating the Candidate Chemical's presence in the indoor and outdoor environment, biota, humans (e.g., biomonitoring studies), human food, drinking water, and other media; and (iii) evidence of persistence, bioaccumulation, lactational, and transplacental transfer.

See Section 3.2.2 for additional information.

Studies have documented the presence of toluene in nail salons' indoor air, demonstrating potential exposure to workers, patrons, and visitors. Nail products containing toluene are opened to allow for application, resulting in the volatilization of the Candidate Chemical into the indoor air being breathed by nail technicians and their customers. Building parameters, air exchange rates, ventilation, weather conditions, seasonal variations (Grešner et al. 2016), and the use of personal protective equipment (OSHA 2017; Quach et al. 2012; Quach et al. 2013) all affect toluene exposure potential. Ventilation is a critical factor in determining indoor air conditions and potential exposure to workers and consumers. While adequate ventilation reduces worker exposure, many salons don't have it (Goldin et al. 2014; NYSDOH 2016). In one study, only eight of 22 nail salons in the Boston area had mechanical ventilation systems (Roelofs and Do 2012). Respiratory problems from chemical exposure are made worse by inadequate ventilation in salons (Marlow et al. 2012). While inhalation is the primary exposure route for toluene in nail products, people may also be exposed to toluene dermally via nail product application and accidental spillages, and orally from accidental ingestion and hand-to-mouth behavior such as nail biting (Rister 2016).

Published studies show detected toluene concentrations in nail salons' indoor air and in the breathing zone of nail salon workers.

Published studies show detected toluene concentrations in nail salons' indoor air and in the breathing zone of nail salon workers. In a study of 30 nail salons throughout California, median and 90 percent upper confidence limit (UCL) on the arithmetic mean indoor air toluene concentrations were 100 and 138 ppb (380 $\mu\text{g}/\text{m}^3$ and 520 $\mu\text{g}/\text{m}^3$). Additionally, the median and 90 percent UCL on the arithmetic mean for personal air monitoring of nail salon technicians were 200 and 260 ppb (754 and 980 $\mu\text{g}/\text{m}^3$) (McNary and Jackson 2007). One researcher sampled indoor air over a four-hour duration in a number of Los Angeles-area nail salons and detected toluene in 75 percent of the salons (Nguyen 2016). The highest detected toluene concentration of 130 ppb (490 $\mu\text{g}/\text{m}^3$) was above the chronic OEHHA REL (Nguyen 2016).

Beyond California:

- Alaves et al. (2013) detected a maximum concentration of toluene in indoor air at nail salons in Salt Lake County, Utah, of 300 ppb (1,130 $\mu\text{g}/\text{m}^3$). This toluene concentration level exceeds the chronic OEHHA REL.
- Hollund and Moen (1998) detected toluene in indoor air in Norwegian nail salons at a range of 40 to 110 $\mu\text{g}/\text{m}^3$ (10 to 30 ppb).
- Tsigonia et al. (2010) detected a maximum of 67 $\mu\text{g}/\text{m}^3$ (17 ppb) of toluene in indoor air at three nail salons. This detection was not greater than the chronic OEHHA REL.
- Peters et al. (2007) detected toluene at a six-day mean time-weighted average concentration of 100 ppb (380 $\mu\text{g}/\text{m}^3$) in nail salons in Brisbane, Australia, thus exceeding the chronic OEHHA REL.
- Park et al. (2014) detected high concentrations of toluene in indoor air at Korean nail salons. They detected an arithmetic mean of 95,400 ppb (359,520 $\mu\text{g}/\text{m}^3$) and a maximum of 490,000 ppb (1,846,570 $\mu\text{g}/\text{m}^3$) toluene in indoor air (Park et al. 2014). These detections greatly exceeded the chronic OEHHA REL but may not be representative of indoor air conditions in California nail salons.

DTSC compared concentrations of toluene in indoor air to the OEHHA-established chronic REL for toluene in indoor air (OEHHA 2016). See Table 3 and Figure 4.

Table 3. Maximum detected concentrations of toluene in indoor air studies

Concentration ($\mu\text{g}/\text{m}^3$)	Concentration (ppb)	Reference
490	130	(Nguyen 2016)
520*	138*	(McNary and Jackson 2007)
1,130	300	(Alaves et al. 2013)
110	30	(Hollund and Moen 1998)
67	17	(Tsigonia et al. 2010)
380	100	(Peters et al. 2007)
1,846,570**	490,000**	(Park et al. 2014)

*This concentration is the 90% UCL on the arithmetic mean.

** This value may not be representative of indoor air conditions of nail salons in California.

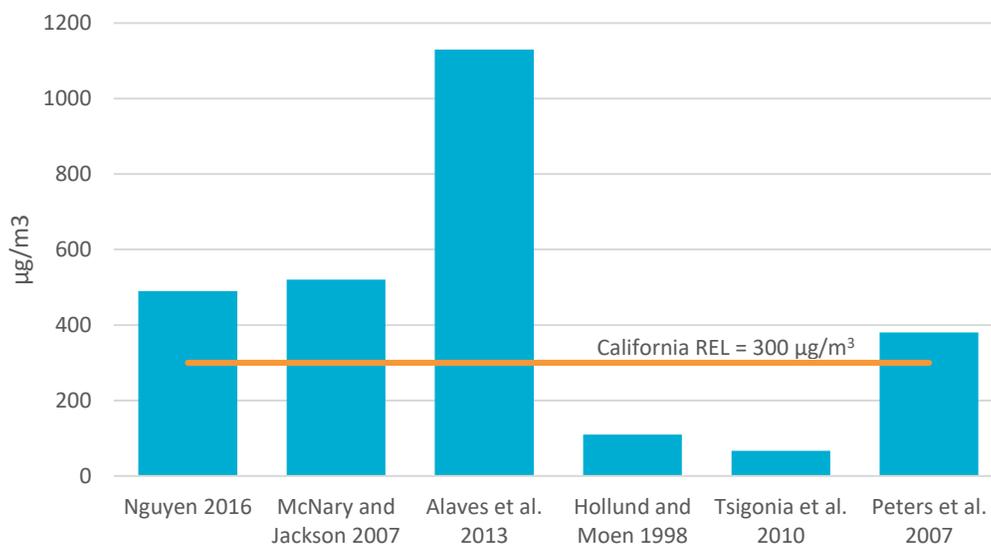


Figure 4. Detected maximum concentrations of toluene in indoor air studies compared to the California REL (300 µg/m³)

In 20 Alameda County nail salons, Quach et al. (2011) measured the exposure of 80 workers to toluene, methyl methacrylate, and total VOCs using personal air monitors. The average measured toluene level of 150 ppb (560 µg/m³) was nearly twice OEHHA's chronic inhalation REL of 300 µg/m³. Twenty-one percent of surveyed nail technicians in this study reported nose, throat, lung, skin, or eye irritation (Quach et al. 2011). In two other studies in Bay Area nail salons, toluene was measured in the personal air samples of all salon workers tested (Garcia et al. 2015; Quach et al. 2013).

As mentioned in Section 3.2.2, Curry et al. (1994) measured indoor air concentrations of toluene during at-home use of nail coating products at five different residences in California. The mean toluene levels measured in air during the nail coating application ranged from 3,200 to 9,200 µg/m³ (850 to 2,400 ppb), while the post-application concentrations ranged from 200 to 1,700 µg/m³ (50 to 450 ppb). Toluene was not detected in any air samples above the detection limits of 200 µg/m³ (50 ppb) prior to the nail coating application (Curry et al. 1994).

3.3.2 Potential exposure to the Candidate Chemical during the product's life cycle

Reference: CAL. CODE REGS. tit. 22, § 69503.3(b)(4)(A).

Potential exposures to the Candidate Chemical or its degradation products may occur during various product life cycle stages, including manufacturing, use, storage, transportation, waste, and end-of-life management practices. Information on existing regulatory restrictions, product warnings, or other product use precautions designed to reduce potential exposures during the product's life cycle may also be discussed here.

See Section 3.2, Section 3.3.1, Section 3.3.3, Section 3.4, and Section 3.5 for additional information.

Nail products are manufactured in industrial facilities in California, other U.S. states, and worldwide. While workers in such facilities are potentially exposed to toluene during the manufacture of nail products, this

evaluation of toluene in nail products is focused on exposure to nail industry workers and nail product consumers.

There is also the potential for indoor air contaminants, such as toluene, to migrate into adjacent buildings, businesses, and residents. In one case, a single large shopping center building was sampled for VOCs in indoor air and provided several lines of evidence suggesting that detected toluene and acetone originated from adjoining salons (Eklund et al. 2008).

3.3.3 Frequency, extent, level, and duration of potential exposure for each use and end-of-life scenario

Reference: CAL. CODE REGS. tit. 22, § 69503.3(b)(4)(E).

Frequency of product use (how often), and the extent (the number of routes of exposure), level (concentration of the Candidate Chemical), and duration (length of time) of use, are all considered when assessing the potential for exposure to the Candidate Chemical or its degradation products.

See Section 3.2, Section 3.3.1, Section, 3.3.2, Section 3.4, and Section 3.5 for additional information.

A variety of nail products contain toluene, including nail polishes and other coatings, nail hardeners, and nail polish thinner (CDPH 2017; EWG 2017; FDA 2017; Mintel 2018). Zhou et al. (2016) detected toluene in 26 out of 34 nail products analyzed, including base coat, top coat, nail polish thinner, gels, remover, and nail polish products, at concentrations ranging from 1.36 to 173,000 ppm ($\mu\text{g/g}$ by weight) (up to 17.3 percent toluene content). In a study conducted by DTSC, 10 of 12 nail coating products labeled “toluene-free” contained toluene at concentrations as high as 177,000 ppm (17.7 percent) (DTSC 2012). Further, eight of 13 nail coating products that made no claims to be toluene-free contained toluene at levels ranging from 110 to 120,000 ppm (0.011 percent to 12 percent) (DTSC 2012).

During product use, nail salon workers and consumers may be exposed to toluene in nail products via inhalation, dermally, or orally. Exposure to toluene via inhalation is well-studied and is more toxicologically significant than other exposure routes due to increased body absorption and distribution of inhaled toluene and its ability to cause or contribute to toxicological endpoints (ATSDR 2017; U.S. EPA 2005b). However, dermal and oral exposure to toluene in nail products also represent exposure pathways of toxicological concern.

Exposure of nail salon workers is influenced by the number of hours worked each week, the number of clients served in a day, the number of nail technicians providing services, the number of times toluene-containing nail products are opened or applied, and the concentration of toluene present in the nail products. Nail industry workers may be exposed to these products daily, potentially several times per day and multiple times per week. Workers in the nail industry often work hours in excess of a standard forty-hour workweek or an eight-hour workday (Quach et al. 2008). During those long work hours, nail salon workers are exposed to multiple nail products simultaneously that may contain toluene. This may result in a greater exposure over an occupational lifetime. One study showed a positive correlation between the number of nail services performed during a given workday and indoor air concentrations of toluene (Nguyen 2016).

Factors affecting indoor air dynamics also contribute to concentrations of toluene in nail salons and result in worker exposures. Building dimensions, room ventilation, weather conditions, air exchange rates, and time of day also play a role in the concentration of toluene present in indoor air (OSHA 2017; Quach et al. 2012; Quach et al. 2013). Ventilation is the preferred exposure control method in nail salons; however, nail salons often lack adequate ventilation and, consequently, have toluene concentrations above acceptable exposure limits. Poor ventilation may be related to lack of or inefficient heating, ventilation, and air conditioning (HVAC) systems combined with the use of inadequate filters (Bennett et al. 2012).

Even with adequate ventilation, salons with several nail technicians performing services simultaneously can lead to elevated levels of VOCs in indoor air.

Even with adequate ventilation, salons with several nail technicians performing services simultaneously can lead to elevated levels of VOCs in indoor air (Nguyen 2016). When adequate ventilation is not possible, the use of personal protective equipment (PPE) by nail technicians can reduce their exposure to toluene. The use of appropriate gloves reduces dermal exposure, and the use of half-facepiece air purifying respirators with organic vapor filtering cartridges reduces inhalation exposure (see Section 3.5.2) (OSHA 2017).

Similar factors influence a consumer's home use exposure to toluene in nail products. At-home nail product use is expected to cause less toluene exposure based on the number of times nail products are used in each day or week. However, indoor air dynamics, room size, ventilation, and the lack of at-home use of PPE could impact exposure and the likelihood of adverse impacts (SCCP 2008).

3.4 Potential Cases of Exposure to the Candidate Chemical in the Product from Various Life Cycle Segments – Special Situations

This section would be used to discuss potential exposures to a Candidate Chemical used in products that 1) may be made in, stored in, or transported through California but are not used in the state, or 2) are exempted from the statutory definition of a consumer product. Nail products with toluene do not meet either of these criteria; therefore, this section does not apply.

3.5 Factors That May Mitigate or Exacerbate Exposure to the Candidate Chemical

3.5.1 Containment of the Candidate Chemical within the product

Reference: CAL. CODE REGS. tit. 22, § 69503.3(b)(4)(F).

When assessing the exposure potential, the SCP regulations consider how the Candidate Chemical is contained or bound during product use (e.g., as an inaccessible component inside a product) and the degree to which the containment is protective at end-of-life (e.g., recycling or disposal).

Nail products are formulated mixtures of chemicals that include toluene as a solvent. Due to its high vapor pressure, toluene readily volatilizes at ambient and room temperatures, and it is potentially released from nail products during product use and end-of-life.

3.5.2 Engineering and administrative controls that reduce exposure concerns

Reference: CAL. CODE REGS. tit. 22, § 69503.3(b)(4)(G).

The SCP regulations also consider any administrative controls (e.g., warning labels on a product) or engineering controls (e.g., specialized ventilation equipment) that can reduce the potential for chemical exposures from the product during product manufacturing, use, or end-of-life.

Occupational exposures to harmful substances should be addressed via a well-documented hazard control methodology widely accepted by industrial hygiene professionals and safety organizations. CDC's National Institute for Occupational Safety and Health (NIOSH) recommends following a hierarchy of controls to protect workers from hazards in order of preference:

- 1) elimination of the hazard;
- 2) substitution with a different chemical;
- 3) engineering controls, including processes and systems such as exhaust ventilation, which are designed to remove a hazard at the source, to reduce or eliminate worker exposure;
- 4) administrative controls, including the implementation of policies, procedures, and employee training; and
- 5) the use of PPE (NIOSH 2016).

Eliminating a chemical hazard entirely, or substituting a less hazardous chemical, is the most effective means of minimizing potential occupational exposures to workers. Engineering controls can also be effective, especially when combined with administrative controls and PPE. However, administrative controls and PPE are the least desirable approaches to control potential occupational exposure, because the original hazard is still present in the workplace (NIOSH 2016).

Nail industry workers are frequently exposed to volatile chemicals in nail salons (Quach et al. 2011). Nail salon workers typically work in small business establishments (e.g., a mean size of 512 square feet and mean volume of 5,882 cubic feet in California) that are poorly ventilated, and some salons are built in enclosed buildings such as indoor malls and high-rises (Quach et al. 2011).

If toluene-containing products cannot be avoided, it is crucial to follow engineering controls to reduce chemical exposure in nail salons. Proper ventilation reduces nail salon workers' exposure to airborne chemicals (NYSDOH 2016). NIOSH and OSHA recommend proper ventilation systems as an engineering control to reduce exposure to toluene and other chemicals (NIOSH 1999; OSHA 2012). However, many salons in California do not have adequate ventilation. In one study of 20 nail salons in Alameda County, California, only 8 percent of nail salons had table ventilators. Higher VOC levels were measured in the breathings zone of nail technicians who worked in nail salons without table ventilators (Quach et al. 2011). A study of 21 nail salons in Boston had similar findings: 15 of the salons (71 percent) had measured CO₂ levels exceeding 800 ppm, suggesting that these salons have insufficient ventilation; these salons had elevated levels of total VOCs and 2.5 µm particulate matter as compared with well-ventilated salons (Goldin et al. 2014).

Ventilation control systems fall into two main categories: local exhaust ventilation (LEV) and dilution ventilation. LEV systems aim to capture contaminants at or near the source of release and remove them before they can be

inhaled by workers or others (NYSDOH 2016). LEV systems include downdraft ventilated tables (NIOSH 1999), portable source capture ventilation (SCV) systems, and ventilation systems that remove contaminants before they cross the breathing zone (Marlow et al. 2012). Dilution ventilation systems reduce contaminant concentrations within the room or area but do not remove the contaminant at its source. Dilution ventilation primarily provides conditioned air to an area for general comfort and odor control (NYSDOH 2016).

A 2012 NIOSH study examined the effectiveness of various SCV systems in nail salons (Marlow et al. 2012). Three different exhaust systems and four different collecting hoods were tested under controlled laboratory conditions. On average, the SCV systems reduced exposures by 50 to 60 percent (Marlow et al. 2012). Based on these findings, NIOSH recommends placing LEV units close to the area where artificial nail services are done, or performing nail services at ventilated work tables and exhausting this air to outside (NIOSH 1999). OSHA also recommends that salons use portable ventilation machines to remove dust and chemicals from the breathing zones of nail salon workers and their customers in order to reduce their chemical exposure (OSHA 2012).

An air monitoring study in California nail salons confirms the benefits of LEVs; salons with table ventilators had significantly lower levels of volatile chemicals in the air than salons that did not use them (Quach et al. 2011). Salons that used other forms of ventilation, including opening doors and windows, using table fans, and installing roof fans, had lower concentrations of VOCs in their air than salons that did not follow these practices (Quach et al. 2011). Further, nail salons located in enclosed buildings (e.g., high-rises or indoor malls) had higher measured concentrations of VOCs in indoor air (Quach et al. 2011).

Nail salons can implement a variety of other engineering and administrative controls to reduce exposure to toluene and other VOCs from nail products. They include:

- installing exhaust fans that pull air from one end of the salon and push it out of the salon, and always keeping the exhaust system on (OSHA 2012; OSHA 2017);
- always keeping the HVAC system on during work hours and replacing the filter once per year (OSHA 2012; U.S. EPA 2007);
- changing charcoal filters of ventilated tables at least once a month and cleaning out the catch basins at least once a week (OSHA 2012; OSHA 2017; U.S. EPA 2007);
- opening doors and windows (OSHA 2012; OSHA 2017a);
- using less toxic products (OSHA 2012; Quach et al. 2012);
- reading product labels and Safety Data Sheets and following manufacturers' instructions when using all nail salon products (OSHA 2012; OSHA 2017; U.S. EPA 2007);
- storing chemicals in small bottles with small openings and labeling them with information from the manufacturer's label (OSHA 2012; U.S. EPA 2007);
- closing chemical bottles tightly when they are not being used, and not keeping extra product at workstations (OSHA 2012; OSHA 2017; U.S. EPA 2007);
- using metal trashcans with tight, self-closing lids (OSHA 2012; U.S. EPA 2007);
- following instructions and applicable hazardous waste regulations when disposing of used or unwanted chemicals (OSHA 2012; OSHA 2017; U.S. EPA 2007);
- training nail technicians in their native language on techniques and procedures to reduce workplace chemical exposures (Quach et al. 2013);

- taking regular breaks outside the salon (OSHA 2012; Quach et al. 2012);
- washing hands between clients and before eating, drinking, putting on cosmetics, and smoking (OSHA 2012; U.S. EPA 2007);
- keeping food and drinks covered at all times, and not storing or eating food in work areas (OSHA 2012; U.S. EPA 2007); and
- using PPE including protective eyewear or goggles, nitrile gloves, NIOSH-approved filtering facepiece respirators also known as N95 masks¹⁴ (OSHA 2017; Quach et al. 2013; U.S. EPA 2007).

Using half-facepiece air purifying respirators (APRs) with organic vapor filtering cartridges (which offer protection from breathing in chemical vapors) can also protect workers from hazardous gases and vapors when performing tasks such as moving chemicals from large bottles to smaller bottles and cleaning up large spills. Use of APRs requires that the employer implement a respiratory protection program under U.S. Occupational Safety and Health Administration (OSHA) Respiratory Protection Standard 29 CFR 1910.134, which has certain requirements including training and fit testing. Further, employers must evaluate the appropriate cartridges for the job, provide cartridges to workers, and inform workers of how and when to change cartridges (OSHA 2017).

While proper use of appropriate PPE can reduce toluene exposure from nail products, nail technicians are inconsistent in their use of PPE, and many technicians rarely or never use it.

While proper use of appropriate PPE can reduce toluene exposure from nail products, nail salon owners may not provide such PPE, and their use is inconsistent among nail technicians and many technicians rarely or never use it. In one survey, 66 percent of nail technicians indicated that they wear gloves at least sometimes when using nail products; however, most said they do not wear additional protective gear such as face masks or protective eyewear (Nails Magazine 2015). A study of nail technicians in Manhattan found that 415 out of 562 respondents (74 percent) were not wearing gloves despite legislation in New York requiring them to do so (Basch et al. 2016). A survey of 65 nail technicians in Oregon had similar findings; 72 percent and 32 percent, respectively, rarely or never use gloves and masks (White et al. 2015). Moreover, customers including pregnant women, their fetuses, and children that receive nail services do not wear PPE and are at risk of being exposed to toluene.

Even when nail technicians do wear PPE, they often use equipment that is not appropriate for the chemicals that are present in their workplaces. Goldin et al. (2014) found that some nail salon workers wear surgical masks as PPE, even though these masks do not prevent exposure to chemical vapors or particulates. Salon workers may also choose gloves that do not protect against toluene exposure.

A recent in-person health and safety survey of nail technicians revealed a need for better training and availability of appropriate PPE (Shendell et al. 2018). Improved training combined with a better dissemination of information can reduce risks to workers and the likelihood of adverse effects associated with occupational exposures (Quach et al. 2013; Roelofs et al. 2007; White et al. 2015). A 2015 paper describes a health and safety

¹⁴ N95 masks help protect from dust, viruses, and germs. They do not provide protection from vapors or gases. Some N95s have filters that reduce chemical odors, but they may not protect from harmful chemical exposure levels.

training program for cosmetology students that focused on chemical hazards and risks in the workplace; after participating in the programs, trainees had increased knowledge, improved safety practices, and enhanced communication about health and safety (Mayer et al. 2015). In 2018, DTSC published Healthy Nail Salon Recognition (HNSR) Program Guidelines to improve nail salon safety and health statewide in California (DTSC 2018b). DTSC's HNSR program guidelines include training topics for salon workers such as use of PPE; adopting safer products; safe chemical handling, transfer, storage, and disposal; and implementing proper ventilation (DTSC 2018b). While better, more consistent training of salon staff may reduce toluene exposures to nail salon workers and their clients, the potential for exposure exists even in salons that have implemented such training programs.

Discussion Draft

4 ADVERSE WASTE AND END-OF-LIFE EFFECTS

Reference: CAL. CODE REGS. tit. 22, §§ 69503.2(b)(1)(B) and 69501.1(a)(8).

DTSC is most concerned about toluene exposures during the use phase. While toluene in discarded nail products can be released to the environment, the products are generally packaged in relatively small containers, limiting the amount of toluene released from an individual product. Toluene released from disposed nail products is expected to be diluted in ambient air or in wastewater and degraded by the processes discussed in Section 2.2.1. Consequently, DTSC is not basing its proposal on this factor.

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5 ADDITIONAL CONSIDERATIONS

This Section summarizes other relevant information not captured under the adverse impact and exposure factors named in section 69503.3 of the Safer Consumer Products regulations.

5.1 Other Relevant Factors Not Identified by the Regulation

In 2012, DTSC performed an investigation of nail products from California distributors and analyzed select products for metals, volatile, and semi-volatile compounds. This effort was focused on three chemicals used in nail products which have clear hazard traits – formaldehyde, toluene, and DBP – which are commonly referred to as the “toxic trio.” This study found that a number of products advertised as “3-free” (i.e., free of formaldehyde, toluene, and DBP) actually contained DBP, toluene, or both (DTSC 2012). This study also detected other chemicals in the tested nail products, including some on the Safer Consumer Products Candidate Chemical list. While nail product manufacturers appear to have largely phased out use of formaldehyde and DBP, some nail products still contain toluene.

In the U.S. and Europe, market trends are moving toward minimizing or eliminating the use of certain chemicals in nail products. For example, Walmart has asked its suppliers to remove toluene from their products. Under the Walmart policy, manufacturers must list the targeted ingredients on packaging by 2018 and work to find alternatives (Coleman-Lochner and Martin 2016).

Other recent efforts in California have focused on nail product safety. In 2012, the San Francisco Department of the Environment (SF Environment) created a voluntary recognition program for nail salons that choose safer alternative chemicals in nail products, train their employees on safer practices that reduce exposure, provide and require employees to use personal protective equipment, and improve indoor air quality by installing mechanical ventilation units (SF Environment 2018). Since then, several other counties and cities have established voluntary Healthy Nail Salon Programs that recognize salons that use less toxic polishes and other nail products, improve ventilation, and participate in trainings that focus on best practices for a healthier workplace (CHNSC 2018).

In addition to voluntary recognition programs established by local jurisdictions, several recent California laws focus on the health, safety, and education of nail salon workers statewide:

AB 2125 (2015-2016) – The Healthy Nail Salon Recognition Program (Health & Saf. Code § 25257.2)

- Includes recognizing businesses that use less toxic nail polishes and polish removers and improve ventilation.
- Calls upon DTSC to publish guidelines for cities and counties to implement voluntary local Healthy Nail Salon Recognition (HNSR) programs, including a list of chemicals that should not be used by salons seeking HNSR program recognition.¹⁵

¹⁵ DTSC published the [Healthy Nail Salon Recognition Program Guidelines](#) in April 2018.

AB 2025 (2015-2016) – Barbering and Cosmetology: Labor Law Education Requirements (amended Bus. & Prof. Code §§ 7312, 7314, 7314.3, 7337, 7347, and 7389)

- Provides for improved education and language access for salon workers.

AB 2437 (2015-2016) – Barbering and Cosmetology: Establishments: Posting Notice (Bus. & Prof. Code § 7353.4)

- Requires salons to post notices regarding workplace rights and wage and hour laws in English, Spanish, Vietnamese, and Korean.

5.2 Key Data Gaps

DTSC has not identified specific data gaps that impact the proposal for this listing.

5.3 Conflicting Studies

The European Commission’s Scientific Committee on Consumer Products (SCCP) concluded that occasional at-home consumer toluene exposure from nail products, in the range of 1 to 4 ppm, can be considered as safe (SCCP 2008). This opinion is based on the assumptions that exposure duration is less than 30 minutes, toluene air levels are 1 to 4 ppm in nonventilated rooms during at-home use, or client toluene exposure in ventilated nail salons is 0.26 ppm or less. This conclusion is based on an exposure-driven evaluation of both acute inhalation effects and reproductive toxicity. The SCCP did not evaluate nail salon workers in its assessment.

6 DISCUSSION OF POTENTIAL FOR SIGNIFICANT OR WIDESPREAD ADVERSE IMPACTS

This Section integrates the information provided in the profile to demonstrate how the key prioritization principles, as identified in the SCP regulations, are met.

DTSC has determined that exposure to toluene through normal use of nail products may contribute to or cause significant or widespread adverse impacts to Californians, including sensitive subpopulations such as nail salon workers, pregnant women and their fetuses, infants, children, and adolescents. This determination is based on toluene's volatility and potential for inhalation exposure in nail salons and at home, the hazard traits associated with toluene, and data showing measured toluene levels in air samples collected in homes and nail salons.

Exposure to toluene through normal use of nail products may contribute to or cause significant or widespread adverse impacts to Californians.

Nail products and professional manicure/pedicure services that may expose salon workers and customers to toluene are very popular. In California there are over 9,000 nail salons (Nails Magazine 2017) and more than 130,000 licensed manicurists (DCA 2017). While nail salon workers and consumers may be exposed to toluene via dermal contact or ingestion, inhalation is the most significant exposure route (ATSDR 2017; U.S. EPA 2005b). Toluene is used as a solvent in several nail coating and nail polish thinner products (CDPH 2017; EWG 2017; FDA 2017; Mintel 2018). Building size, room dimensions, air exchange rates, ventilation, and weather conditions influence the concentration of toluene in salon air and, consequently, level of inhalation exposure for nail salon workers and consumers (Quach et al. 2008).

Toluene is a liquid at room temperature and readily volatilizes into indoor air (HSDB 2016). Several studies conducted in nail salons detected toluene at concentrations higher than California's chronic Reference Exposure Levels (Alaves et al. 2013; Hollund and Moen 1998; McNary and Jackson 2007; Nguyen 2016; Park et al. 2014; Tsigonia et al. 2010). Further, a personal air monitoring study of 80 workers from 20 nail salons in California detected toluene and other VOCs in salon workers' breathing zones (Quach et al. 2011).

In addition to being a neurotoxicant, toluene is a developmental toxicant with potential to affect unborn fetuses (see Section 2.3). Research studies suggest that toluene exhibits other hazard traits including neurodevelopmental toxicity, respiratory toxicity, liver toxicity, and kidney toxicity. Toluene has also been linked to immunotoxicity and vision and hearing impairment (see Section 2.3).

Nail salon workers' potential for exposure to toluene is exacerbated by several factors: They often work in excess of eight-hour days or 40-hour weeks; they are often not provided with adequate information concerning chemical safety; they are often not provided with proper PPE; and their workplaces often lack appropriate ventilation (Quach et al. 2008). Pregnant nail technicians and their fetuses are especially sensitive to adverse impacts of toluene exposure from nail products (see Section 2.5.2). Infants and children of nail technicians often accompany their parents to the workplace and may be exposed to toluene-containing nail products. Even if they are not directly exposed to toluene-containing nail products, nursing infants and children may be exposed to

toluene, as indicated by detected toluene in human milk (Fabietti et al. 2004). Infants and young children are more susceptible than adults to adverse impacts from toluene due to physiological differences (see Section 2.5.2). Chemical exposure of nail industry workers is an environmental justice issue, as a large majority of nail industry workers are people of color and lower socioeconomic status.

7 ALTERNATIVES

Reference: CAL. CODE REGS. tit. 22, § 69503.2(b)(3).

This Section summarizes information available to DTSC regarding alternatives that may or may not be safer than the Candidate Chemical. DTSC does not need to ensure that these alternatives are safer and may summarize their associated hazards to illustrate readily available information. The Sections below may include information such as how readily available an alternative is, product functions addressed by the alternative, and implications for manufacturers using the alternative (e.g., use limitations, product reformulation, different equipment needs).

Some of the alternative solvents to toluene currently used in nail products include ethyl acetate, butyl acetate, isopropanol (IPA), methyl ethyl ketone (MEK), and water. IPA and MEK are, like toluene, Candidate Chemicals. DTSC has summarized some readily available information on use in nail products and associated hazard traits but has made no determination about their safety relative to toluene. This Section is not intended to be an exhaustive list of alternatives; there are other known chemical alternatives to toluene that are not described below.

7.1 Chemical Alternatives

7.1.1 Chemical Name: Ethyl Acetate

Discussion of applicability of the chemical alternative:

Ethyl acetate is a colorless liquid used as solvent in nail polish, base coats, nail polish removers, and other nail products (CIR 1989; HSDB 2015). It is volatile, soluble in water, and naturally occurs in many foods (HSDB 2015). The specifications of CARB's Consumer Products regulations prohibit ethyl acetate use in nail polish removers in California (CARB 2015).

Readily available hazard trait and exposure information:

Acute to chronic ethyl acetate exposure can result in respiratory dysfunction and eye, nose, and throat irritation. Higher concentrations can cause central nervous system effects such as headaches, sleepiness, and unconsciousness. Animals administered very high doses experienced decreased body and organ weights as well as decreased appetite (HSDB 2015). Animal data does not indicate that ethyl acetate is a skin irritant or sensitizer (CIR 1989; HSDB 2015).

Nail salon workers may potentially be exposed to ethyl acetate from nail products. Ethyl acetate was measured in 74 salons' indoor air in Norway at a concentration range of 0.01 to 1.19 ppm (Gjølstad et al. 2006).

Ethyl acetate readily volatilizes and rapidly degrades when released to the environment. Ethyl acetate is expected to evaporate rapidly from water and soil and is unlikely to adsorb to suspended solids and sediment. Ethyl acetate is biodegradable and is not expected to build up in aquatic organisms (HSDB 2015).

7.1.2 Chemical Name: Butyl Acetate

Discussion of applicability of the chemical alternative:

Butyl acetate is a clear colorless chemical used as a solvent in the production of lacquers and as a flavoring agent (IPCS 2005). It is used as a solvent across a wide variety of products including nail polish, nail polish removers, base coats, and other nail products (Arora and Tosti 2017; CIR 1989).

The specifications of the CARB Consumer Products regulations prohibit butyl acetate's use in nail polish removers in California (CARB 2015).

Readily available hazard trait information:

Butyl acetate is a minor respiratory irritant when inhaled and can cause minor irritation to the eyes (HSDB 2012). When tested at an unspecified concentration and up to 25.5 percent in cosmetic formulations, butyl acetate was, at most, a mild irritant and was not a sensitizer to humans (CIR 1989). Butyl acetate primarily volatilizes to the atmosphere when released to the environment, where it will react with hydroxyl radicals and undergo photochemical oxidation. It is readily biodegradable and does not bioaccumulate in aquatic organisms (IPCS 2005).

7.1.3 Chemical Name: Isopropanol

Discussion of applicability of the chemical alternative:

Isopropanol (IPA), commonly referred to as isopropyl alcohol, is an alcohol used as a solvent in nail polish and other coatings (CDPH 2017; EWG 2017; Mintel 2018).

Readily available hazard trait information:

IPA is listed as a Candidate Chemical (DTSC 2018a), and listed with inhalation or oral reference exposure levels by OEHHA. OEHHA identified noncancer endpoints of developmental toxicity, kidney toxicity, ocular toxicity, and respiratory toxicity (OEHHA 2016).

In animal studies, pups of pregnant rats that inhaled IPA showed decreases in fetal weight in a dose-dependent manner and developmental toxicity at very high doses (Nelson et al. 1988).

7.1.4 Chemical Name: Methyl Ethyl Ketone

Discussion of applicability of the chemical alternative:

Methyl ethyl ketone (MEK) is a solvent used in nail products including nail coatings and nail polish thinner (EWG 2017; Mintel 2018).

Readily available hazard trait information:

MEK is identified as a toxic air contaminant by CARB for developmental toxicity, neurotoxicity, ocular toxicity, and respiratory toxicity (CARB 2011). MEK is also identified with noncancer endpoints for ocular and respiratory toxicity and listed with inhalation and oral reference exposure levels by OEHHA (OEHHA 2016).

In utero exposure to MEK causes developmental toxicity; in animals, studies have shown decreases in pup weights, organ weights, and skeletal anomalies (U.S. EPA 2003). Most human studies have focused on solvent abuse (intentional inhalation) and occupational exposures other than in nail salons, where inhalation and dermal exposures to high doses of MEK occurred (up to 100 percent MEK solvent) (U.S. EPA 2003). Many other occupational exposures to MEK occur with a mixture of other solvents, so it is not possible to relate observed hazards specifically to MEK exposure (U.S. EPA 2003). Studies with volunteers suggest MEK may also be a respiratory tract irritant at high doses (OEHHA 2008).

7.1.5 Chemical Name: Water

There are some advantages and disadvantages to water-based nail polishes. Water-based nail polishes do not contain toxic solvents, but they may not last as long as traditional solvent-based polish. Challenges with water-based polish include longer drying time, difficulty hardening the polish, lack of polish brilliance, and lack of polish adherence to the nail (Malnou 2014).

7.2 Non-Chemical alternatives

7.2.1 Discussion of applicability of the non-chemical alternative

Not applicable.

8 OTHER REGULATORY PROGRAMS

Reference: CAL. CODE REGS. tit. 22, § 69503.2(b)(2).

DTSC identified the following state and federal regulatory programs and laws related to the product or the Candidate Chemical in the product that are intended to protect public health and the environment. DTSC has assessed these programs to ensure that they do not overlap or conflict with this proposal to list nail products containing toluene as a Priority Product nor with any subsequent regulation that may result for such listing.

8.1 U.S. Food and Drug Administration

The U.S. Food and Drug Administration (FDA) is authorized by the Federal Food, Drug, and Cosmetic Act (FDCA) to oversee the safety of food, drugs, and cosmetics (FDA 2016). The FDCA does not authorize the FDA to require safety testing of cosmetics, and there is no approval process for cosmetics products prior to sale in the U.S. (except for color additives). However, the FDA can and does inspect cosmetics manufacturing facilities to ensure that cosmetics are not adulterated (FDA 2016).¹⁶

The FDCA does not authorize the FDA to require safety testing of cosmetics, and there is no approval process for cosmetics products prior to sale in the U.S.

While cosmetic product manufacturers are legally responsible for ensuring the safety of their products, neither the FDCA nor FDA regulations require specific tests to demonstrate the safety of individual products or ingredients, and manufacturers are not required to share their safety information with the FDA. However, the FDA can pursue enforcement action against products on the market that it determines are not in compliance with the FDCA or the Fair Packaging and Labeling Act (FPLA), or against firms or individuals who violate these laws (FDA 2016).

8.1.1 Federal Food, Drug, and Cosmetic Act

The FDCA is a set of laws passed by Congress in 1938 giving authority to the FDA to oversee the safety of food, drugs, and cosmetics (FDA 2018). The FDCA defines cosmetics as “articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body ... for cleansing, beautifying, promoting attractiveness, or altering the appearance” (FDA 2016). As noted above, the FDA does not pre-approve cosmetic products. However, cosmetic products must be properly labeled and safe for consumers under labeled or typical conditions of use. The FDCA prohibits the marketing of adulterated or misbranded cosmetics in interstate commerce, and the FDA can remove cosmetics from the market that contain unsafe ingredients or that are mislabeled.

8.1.2 Fair Packaging and Labeling Act

The Fair Packaging and Labeling Act (FPLA) requires each package of household consumer products to bear a label that includes a statement identifying the commodity (detergent, sponge, etc.); the name and place of

¹⁶ “Adulterated” cosmetics refers to product composition violations: whether they result from ingredients, contaminants, processing, packaging, or shipping and handling FDA (2016) FDA Authority Over Cosmetics: How Cosmetics Are Not FDA-Approved, but Are FDA-Regulated. U.S. Food and Drug Administration (FDA). In. <https://www.fda.gov/Cosmetics/GuidanceRegulation/LawsRegulations/ucm074162.htm> Accessed October, 2017 .

business of the manufacturer, packer, or distributor; and the net quantity of contents in terms of weight, measure, or count (in both metric and English units). The FPLA is designed to facilitate value comparisons and to prevent unfair or deceptive packaging and labeling of many household consumer commodities (FDA 2009).

8.2 U.S. Environmental Protection Agency

- Toluene is listed under the Toxic Substances Control Act (TSCA) of 1976, which was enacted by Congress to test, regulate, and screen all chemicals produced in or imported into the United States. TSCA requires any chemical that reaches the consumer marketplace to be tested for possible toxic effect prior to commercial manufacture (U.S. EPA 2018). Under Section 8, TSCA requires reporting and record keeping by persons who manufacture, import, process, and/or distribute chemical substances in commerce. Under Section 8(e), any person who manufactures (which includes importing), processes, or distributes in commerce a chemical substance or mixture and who obtains information which reasonably supports the conclusion that such substance or mixture presents a substantial risk of injury to health or the environment should immediately inform EPA, except in situations where EPA has been adequately informed of such information (40 C.F.R. § 716.120 1994).
- Toluene is listed as a hazardous air pollutant under the Clean Air Act (42 U.S.C. § 7412 1999).
- Toluene is listed as an organic hazardous air pollutant under Federal Code of Regulations 40 C.F.R., Section 63, Subpart F, National Emission Standards for Organic Hazardous Air Pollutants from the Synthetic Organic Chemical Manufacturing Industry (40 C.F.R. §63 2006).

8.3 U.S. Occupational Health and Safety Administration

The U.S. Occupational Health and Safety Administration (OSHA) has set a PEL for workers of 200 ppm for toluene in air averaged over an eight-hour workday (OSHA 1993; OSHA 2018a). OSHA acknowledges that many of its PELs are outdated and inadequate to ensure protection of worker health. Most of OSHA's PELs were issued shortly after adoption of the Occupational Safety and Health Act in 1970 and have not been updated since then. The OSHA PEL for toluene was set in 1971 (OSHA 2018b). Nevertheless, as noted above, changes to occupational exposure limits for a chemical are not among the regulatory response options that DTSC might eventually impose for toluene-containing nail products.

8.4 California Division of Occupational Safety and Health, Cal/OSHA

In 2012, the California Division of Occupational Safety and Health (DOSH), also known as Cal/OSHA, set a permissible exposure limit (PEL) for workers of 10 ppm (37.6 mg/m³) for toluene in air averaged over an eight-hour workday (Cal/OSHA 2018; OSHSB 2012). If DTSC proceeds with rulemaking to list toluene-containing nail products as a Priority Product, the regulations would not affect existing occupational exposure limits like the PEL. DTSC might eventually impose one or more regulatory responses on manufacturers of toluene-containing nail products. However, regulatory responses must be selected from among seven options described in Article 6 of the Safer Consumer Products regulations; changes to occupational exposure limits for a chemical are not among these options.

8.5 California Department of Public Health, California Safe Cosmetics Program

The California Department of Public Health (CDPH) created the California Safe Cosmetics Program (CSCP) in response to the passage of the California Safe Cosmetics Act. Beginning in 2009, cosmetic manufacturers with aggregate sales greater than \$1 million must report to CSCP products they sell in California which have intentionally added chemical ingredients identified as known or suspected carcinogens or reproductive or developmental toxicants by authoritative bodies (CDPH 2016).

While the intention of the Safe Cosmetics Act is to improve access to information about potentially harmful ingredients in cosmetics and to influence the reformulation of some products toward safer alternatives, it does not duplicate the SCP regulations. The Safe Cosmetics Act requires manufacturers to report certain chemical ingredients in products, but it does not require manufacturers to evaluate those products for safer chemical alternatives.

8.6 California Air Resources Board

CARB's Consumer Products regulations restrict the manufacture and sale of specific products that contain volatile organic compounds (VOCs), a broad grouping of chemicals that have the potential to react to form air pollutants including ground-level ozone and particulates (CARB 2014; CARB 2015; CARB 2018). Under these regulations, no person shall sell, supply, offer for sale, or manufacture for sale in California any nail polish remover which, at the time of sale or manufacture, contains 1 percent VOCs by weight (CARB 2015). Toluene concentrations in removers would greatly exceed 1 percent; thus, toluene is not allowed as a compound in nail polish remover in California (CARB 2017). Acetone has been exempted from the requirements of this regulation (CARB 2015). There are currently no CARB regulations for nail polish or nail polish thinner.

ACRONYMS AND ABBREVIATIONS

Abbreviations used in this document

ATSDR	Agency for Toxic Substances and Disease Registry	IPCS	International Programme on Chemical Safety
Cal/OSHA	California Division of Occupational Safety and Health	IRIS	Integrated Risk Information System
<i>CAL. CODE REGS. tit., §</i>	California Code of Regulations, title, section	LED	light-emitting diode
CARB	California Air Resources Board	LEL	lower explosive limit
CAS	Chemical Abstract Service	LEV	local exhaust ventilation
CDC	Centers for Disease Control and Prevention	MCL	Maximum Contaminant Level
CDPH	California Department of Public Health	MEK	methyl ethyl ketone
CFR	Code of Federal Regulations	MMA	methyl methacrylate
CSCP	California Safe Cosmetics Program	N95 masks	NIOSH-approved filtering facepiece respirators
DBP	dibutyl phthalate	NIOSH	National Institute for Occupational Safety and Health
DCA	Department of Consumer Affairs	NTP	National Toxicology Program
DOSH	California Division of Occupational Safety and Health, also known as Cal/OSHA	NYSDOH	New York State Department of Health
DTSC	Department of Toxic Substances Control	o-cresol	ortho-cresol
EWG	Environmental Working Group	OEHHA	Office of Environmental Health Hazard Assessment
FDA	Food and Drug Administration	OSHA	Occupational Health and Safety Administration
FDCA	Federal Food, Drug, and Cosmetic Act	p-cresol	para-cresol
FPLA	Fair Packaging and Labeling Act	pH	potential hydrogen
GPC	Global Product Classification	PEL	Permissible Exposure Limit
HHS	Department of Health and Human Services	PPE	personal protective equipment
HNSR	Healthy Nail Salon Recognition	Proposition 65 List	chemicals listed as “Known to the State to Cause Cancer or Reproductive Toxicity” under California’s Safe Drinking Water and Toxic Enforcement Act of 1986
HRA	Health Risk Assessment	REL	Reference Exposure Level
HSDB	Hazardous Substances Data Bank	RIVM	National Institute for Public Health and the Environment
HVAC	heating, ventilation, and air conditioning	SCCP	Scientific Committee on Consumer Products
IDLH	immediately dangerous to life and health	SCP	Safer Consumer Products
IARC	International Agency for Research on Cancer	SCV	source capture ventilation
IPA	isopropyl alcohol		

SF Environment SWRCB	San Francisco Department of the Environment State Water Resources Control Board	U.S. EPA	United States Environmental Protection Agency
UEL	upper explosive limit	UV	ultraviolet
UCL	upper confidence limit	VOC	volatile organic compound
		WHO	World Health Organization

Units

atm	atmosphere	K_{ow}	octanol-water partition coefficient
$\text{atm}\cdot\text{m}^3/\text{mol}$	atmosphere times cubic meter per mol	m	meter
$^{\circ}\text{C}$	degrees Celsius	m^3	cubic meter
$^{\circ}\text{F}$	degrees Fahrenheit	mm Hg	millimeter of mercury
ft^2	square feet	mg/L	milligram per liter
ft^3	cubic feet	mg/m^3	milligram per cubic meter
g	gram	nm	nanometer
g/cm^3	gram per cubic centimeter	ppb	parts per billion
g/mol	gram per mol	ppm	parts per million
kg	kilogram	v/v	volume/volume
K_{oc}	organic carbon-water partition coefficient	μg	microgram
		μm	micrometer

REFERENCES

- 40 C.F.R. §63 (2006) Code of Federal Regulations. Title 40: Protection of Environment. Chapter I: Environmental Protection Agency. Part 63- National Emission Standards for Hazardous Air Pollutants for Source Categories. Appendix Table 2 to Subpart F of Part 63, Organic Hazardous Air Pollutants. In: Regulations CoF (ed). vol Title 40, Ch. I, §63,
- 40 C.F.R. § 716.120 (1994) Code of Federal Regulations. Title 40: Protection of Environment. Chapter I: Environmental Protection Agency. Part 716.120 - Substances and listed mixtures to which this subpart applies. In: Regulations CoF (ed). vol Title 40, Ch. I, §716.120,
- 42 U.S.C. § 7412 (1999) 42 U.S. Code § 7412 - Hazardous air pollutants. In: Code US (ed) 42 US Code Title 42: The Public Health and Welfare Chapter 85: Air Pollution Prevention and Control § 7412 - Hazardous air pollutants. vol Title 42, Ch. 85, Sub Chapter I, Part A, § 7412,
- Abbate C, Giorgianni C, Munao F, Brecciaroli R (1993) Neurotoxicity induced by exposure to toluene. An electrophysiologic study. *Int Arch Occup Environ Health* 64(6):389-392
- Aitio A, Pekari K, Jarvisalo J (1984) Skin absorption as a source of error in biological monitoring. *Scand J Work Environ Health* 10(5):317-320
- Alaves VM, Sleeth DK, Thiese MS, Larson RR (2013) Characterization of indoor air contaminants in a randomly selected set of commercial nail salons in Salt Lake County, Utah, USA. *Int J Environ Health Res* 23(5):419-433 doi:10.1080/09603123.2012.755152
- Andersen I, Lundqvist GR, Molhave L, et al. (1983) Human response to controlled levels of toluene in six-hour exposures. *Scand J Work Environ Health* 9(5):405-418 doi:10.5271/sjweh.2393
- Anderson C, Sundberg K, Groth O (1986) Animal model for assessment of skin irritancy. *Contact dermatitis* 15(3):143-151
- Anderson HR, Dick B, Macnair RS, Palmer JC, Ramsey JD (1982) An investigation of 140 deaths associated with volatile substance abuse in the United Kingdom (1971-1981). *Hum Toxicol* 1(3):207-221
- Arnold GL, Kirby RS, Langendoerfer S, Wilkins-Haug L (1994) Toluene embryopathy: Clinical delineation and developmental follow-up. *Pediatrics* 93(2):216-220
- Arnold GL, Wilkins-Haug L (1990) Toluene embryopathy syndrome. *Am J Hum Genet* 47(suppl. 3):A46
- Arora H, Tosti A (2017) Safety and efficacy of nail products. *Cosmetics* 4(4):1-19 doi:10.3390/cosmetics4030024
- Atkinson R (1990) Gas-phase tropospheric chemistry of organic compounds: a review. *Atmos Environ* 24A(1):1-41
- ATSDR (2011) Toxic Substances Portal. Neurological (Nervous System). Toluene. Agency for Toxic Substances and Disease Registry (ATSDR). In. <https://www.atsdr.cdc.gov/substances/toxorganlisting.asp?sysid=18> Accessed July 2017
- ATSDR (2015) Public Health Statement. Toluene. Agency for Toxic Substances and Disease Registry (ATSDR)
- ATSDR (2017) Toxicological Profile for Toluene. Agency for Toxic Substances and Disease Registry (ATSDR)
- Baelum J, Andersen IB, Lundqvist GR, et al. (1985) Response of solvent-exposed printers and unexposed controls to six-hour toluene exposure. *Scand J Work Environ Health* 11(4):271-280 doi:10.5271/sjweh.2221
- Basch C, Yarborough C, Trusty S, Basch C (2016) Use of protective gloves in nail salons in Manhattan, New York City. *J Prev Med Public Health* 49(4):249-251 doi:10.3961/jpmph.16.017
- Battle DC, Sabatini S, Kurtzman NA (1988) On the mechanism of toluene-induced renal tubular acidosis. *Nephron* 49(3):210-218 doi:10.1159/000185057
- Bauer PJ, Pathman T (2008) Memory and Early Brain Development. In: Tremblay RE, Barr RG, Peters RD, Boivin M (eds) *Encyclopedia on Early Childhood Development* [online].
- Bennett DH, Fisk W, Apte MG, et al. (2012) Ventilation, temperature, and HVAC characteristics in small and medium commercial buildings in California. *Indoor Air* 22(4):309-320 doi:10.1111/j.1600-0668.2012.00767.x

- Berenguer P, Soulage C, Perrin D, Pequignot JM, Abiraini JH (2003) Behavioral and neurochemical effects induced by subchronic exposure to 40 ppm toluene in rats. *Pharmacol Biochem Behav* 74(4):997-1003
- Boey KW, Foo SC, Jeyaratnam J (1997) Effects of occupational exposure to toluene: A neuropsychological study on workers in Singapore. *Ann Acad Med Singapore* 26(2):184-187
- Boman A, Hagelthorn G, Magnusson K (1995) Percutaneous absorption of organic solvents during intermittent exposure in guinea pigs. *Acta dermato-venereologica* 75(2):114-119
- Bonzel KE, Müller-Wiefel DE, Ruder H, Wingen AM, Waldherr R, Weber M (1987) Anti-glomerular basement membrane antibody-mediated glomerulonephritis due to glue sniffing. *Eur J Pediatr* 146:296-300
- Bosch X, Campistol JM, Montoliu J, Revert L (1988) Myelofibrosis and focal segmental glomerulosclerosis associated with toluene poisoning. *Hum Toxicol* 7(4):357-561
- Bowen SE, Balster RL (1998) A direct comparison of inhalant effects on locomotor activity and schedule-controlled behavior in mice. *Exp Clin Psychopharmacol* 6(3):235-247
- Bowen SE, Hannigan JH (2013) Binge toluene exposure in pregnancy and pre-weaning developmental consequences in rats. *Neurotoxicol Teratol* 38:29-35 doi:10.1016/j.ntt.2013.04.002
- Bowen SE, Irtenkauf S, Hannigan JH, Stefanski AL (2009) Alterations in rat fetal morphology following abuse patterns of toluene exposure. *Reproductive toxicology (Elmsford, NY)* 27(2):161-169 doi:10.1016/j.reprotox.2009.01.002
- Brookman F (2013) "The Nail Care Battle." *Women's Wear Daily*.
- Brown HS, Bishop DR, Rowan CA (1984) The role of skin absorption as a route of exposure for volatile organic compounds (VOCs) in drinking water. *Am J Public Health* 74(5):479-484
- Bruckner JV, Peterson RG (1981) Evaluation of toluene and acetone inhalant abuse. II. Model development and toxicology. *Toxicol Appl Pharmacol* 61(3):302-312
- Bushnell PJ, Evans HL, Palmes ED (1985) Effects of toluene inhalation on carbon dioxide production and locomotor activity in mice. *Fundam Appl Toxicol* 5(5):971-977
- Cal/OSHA (2018) Title 8, California Code of Regulations, § 5155, Table AC-1, Permissible Exposure Limits for Chemical Contaminants. California Division of Occupational Safety and Health (Cal/OSHA). In. https://www.dir.ca.gov/Title8/5155table_ac1.html Accessed February, 2018
- Callan SP, Kott JM, Cleary JP, McCarthy MK, Baltés BB, Bowen SE (2016) Changes in developmental body weight as a function of toluene exposure: A meta-analysis of animal studies. *Hum Exp Toxicol* 35(4):341-352 doi:10.1177/0960327115591377
- Camara-Lemarrroy CR, Rodriguez-Gutierrez R, Monreal-Robles R, Gonzalez-Gonzalez JG (2015) Acute toluene intoxication--clinical presentation, management and prognosis: A prospective observational study. *BMC Emerg Med* 15:1-7 doi:10.1186/s12873-015-0039-0
- Cao G, Jang M (2008) Secondary organic aerosol formation from toluene photooxidation under various NOx conditions and particle acidity. *Atmos Chem Phys Discuss* 8:14467-14495
- Caravati EM, Bjerk PJ (1997) Acute toluene ingestion toxicity. *Ann Emerg Med* 30(6):838-839
- CARB (2010) An Outdoor Health Risk Assessment of Emissions from Nail Salons. California Air Resources Board (CARB), California Environmental Protection Agency
- CARB (2011) Toxic Air Contaminant Identification List. California Air Resources Board (CARB), California Environmental Protection Agency. In. <https://www.arb.ca.gov/toxics/cattable.htm#Note> and <http://www.dtsc.ca.gov/SCP/upload/2-C-Toxic-Air-Contaminant.pdf> Accessed July, 2017
- CARB (2014) Background. Consumer Products Program. California Air Resources Board (CARB), California Environmental Protection Agency. In. <https://www.arb.ca.gov/consprod/background.htm> Accessed December 2017
- CARB (2015) The California Consumer Products Regulations. California Air Resources Board (CARB), California Environmental Protection Agency
- CARB (2017) Email communication from Joseph Calavita of California Air Resources Board (CARB) to Christine Papagni of DTSC on November 13, 2017.

- CARB (2018) Consumer Products Enforcement. California Air Resources Board (CARB), California Environmental Protection Agency. In. <https://www.arb.ca.gov/enf/consprod.htm> Accessed February 2018
- CDC (2016) Biomonitoring summary. Toluene. Centers for Disease Control and Prevention (CDC). In. https://www.cdc.gov/biomonitoring/Toluene_BiomonitoringSummary.html Accessed October 2017
- CDC (2017) Fourth National Report on Human Exposure to Environmental Chemicals Updated Tables, January 2017, Volume One. Centers for Disease Control and Prevention (CDC)
- CDPH (2016) Cosmetics Containing Ingredients Linked to Cancer or Reproductive Harm. Data Reported to the California Safe Cosmetics Program 2009-2015. California Department of Public Health (CDPH)
- CDPH (2017) California Safe Cosmetics Program Product Database. California Department of Public Health (CDPH). In. <https://safecosmetics.cdph.ca.gov/search/categories.aspx> Accessed October 2017
- Chen HH, Lin YR, Chan MH (2011) Toluene exposure during brain growth spurt and adolescence produces differential effects on N-methyl-D-aspartate receptor-mediated currents in rat hippocampus. *Toxicol Lett* 205(3):336-340 doi:10.1016/j.toxlet.2011.06.026
- CHNSC (2018) Find a Healthy Nail Salon. California Healthy Nail Salon Collaborative (CHNSC). In. <https://cahealthynailsalons.org/find-a-healthy-nail-salon-2/> Accessed February, 2018
- Chouaniere D, Wild P, Fontana JM, et al. (2002) Neurobehavioral disturbances arising from occupational toluene exposure. *Am J Ind Med* 41(2):77-88
- CIIT (1980) A 24 month inhalation toxicology study in Fischer-344 rat exposed to atmospheric toluene. Executive summary and data tables. October 15, 1980. Conducted by Industrial Bio-Test Laboratories, Inc., Decatur, IL, and Experimental Pathology Laboratories, Inc., Raleigh, NC for Chemical Industry Institute of Toxicology (CIIT), Research Triangle Park, NC [As described in ATSDR 2017]
- CIR (1989) Final report on the safety assessment of ethyl acetate and butyl acetate. Cosmetic Ingredient Review Expert Panel (CIR). *J Am Coll Toxicol* 8(4):681-705
- Coleman-Lochner L, Martin A (2016) Wal-Mart Asks Its Suppliers to Stop Using Eight Chemicals. In: Bloomberg. <https://www.bloomberg.com/news/articles/2016-07-20/wal-mart-asks-suppliers-to-remove-eight-chemicals-from-products> Accessed October 2017
- Conti AC, Lowing JL, Susick LL, Bowen SE (2012) Investigation of calcium-stimulated adenylyl cyclases 1 and 8 on toluene and ethanol neurobehavioral actions. *Neurotoxicol Teratol* 34(5):481-488 doi:10.1016/j.ntt.2012.06.005
- Courtney KD, Andrews JE, Springer J, et al. (1986) A perinatal study of toluene in CD-1 mice. *Fundam Appl Toxicol* 6(1):145-154
- Curry KK, Brookman DJ, Whitmyre GK, et al. (1994) Personal exposures to toluene during use of nail lacquers in residences: Description of the results of a preliminary study. *J Expos Anal Environ Epidemiol* 4(4):443-456
- da Silva VA, Malheiros LR, Paumgartten FJR, de Matos Sa-Rego M, Riul TR, Golovattei MAR (1990) Developmental toxicity of in utero exposure to toluene on malnourished and well nourished rats. *Toxicology* 64(2):155-168
- DCA (2017) Email communication from Laurel Goddard of California Department of Consumer Affairs (DCA) to Diana Phelps of DTSC on August 14, 2017.
- DCA (2018) Email communication from Laurel Goddard of California Department of Consumer Affairs (DCA) to Christine Papagni of DTSC on January 26, 2018.
- Deschamps D, Géraud C, Dally S (2001) Cognitive functions in workers exposed to toluene: Evaluation at least 48 hours after removal from exposure. *Int Arch Occup Environ Health* 74(4):285-288
- Dick ALW, Lawrence AJ, Duncan JR (2014) Chronic intermittent toluene inhalation initiated during adolescence in rats does not alter voluntary consumption of ethanol in adulthood. *Alcohol* 48(6):561-569
- Donald JM, Hooper K, Hopenhayn-Rich C (1991) Reproductive and developmental toxicity of toluene: A review. *Environ Health Perspect* 94:237-244
- Drug Store News (2016) "Artificial nails boast consistent growth." *Drug Store News*. vol 38(8), p 88

- DTSC (2012) Summary of Data and Findings from Testing of a Limited Number of Nail Products. Department of Toxic Substances Control (DTSC), California Environmental Protection Agency
- DTSC (2018a) Candidate Chemical Database. Department of Toxic Substances Control (DTSC), California Environmental Protection Agency. In. <http://cit.dtsc.ca.gov/scp/chemicalsearch/ChemicalSearch.aspx> Accessed August, 2018
- DTSC (2018b) Healthy Nail Salon Recognition Program Guidelines. Department of Toxic Substances Control (DTSC)
- Dutkiewicz T, Tyras H (1968) Skin absorption of toluene, styrene, and xylene by man. *Br J Ind Med* 25(3):243
- EC (2003) European Union Risk Assessment Report. Toluene. CAS No. 108-88-3. EINECS No. 203-625-9. European Commission (EC), European Chemicals Bureau
- Echeverria D, Fine L, Langolf G, Schork A, Sampaio C (1989) Acute neurobehavioural effects of toluene. *Br J Ind Med* 46(7):483-495
- Einav S, Amitai Y, Reichman J, Geber D (1997) Bradycardia in toluene poisoning. *J Toxicol Clin Toxicol* 35(3):295-298
- Eklund BM, Burkes S, Morris P, Mosconi L (2008) Spatial and temporal variability in VOC levels within a commercial retail building. *Indoor Air* 18(5):365-374
- Eller N, Netterstrøm B, Laursen P (1999) Risk of chronic effects on the central nervous system at low toluene exposure. *Occup Med (Lond)* 49(6):389-395
- Encyclopædia Britannica (2017) Rotogravure printing. In. <https://www.britannica.com/technology/rotogravure-printing> Accessed March 2018
- Encyclopædia Britannica (2018) Neurotransmitter. In. <https://www.britannica.com/science/neurotransmitter> Accessed July 2018
- Erramouspe J, Galvez R, Fischel DR (1996) Newborn renal tubular acidosis associated with prenatal maternal toluene sniffing. *J Psychoactive Drugs* 28(2):201-204 doi:10.1080/02791072.1996.10524392
- EWG (2017) Environmental Working Group's (EWG) Skin Deep Cosmetics Database. In. <http://www.ewg.org/skindeep#.WhXRcOSWzIU> Accessed November, 2017
- Fabietti F, Ambruzzi A, Delise M, Sprechini MR (2004) Monitoring of the benzene and toluene contents in human milk. *Environ Int* 30(3):397-401 doi:10.1016/j.envint.2003.09.007
- FDA (2009) Fair Packaging and Labeling Act. Title 15 - Commerce and Trade Chapter 39 - Fair Packaging and Labeling Program. Food and Drug Administration (FDA). In. <https://wayback.archive-it.org/7993/20170722051950/https://www.fda.gov/RegulatoryInformation/LawsEnforcedbyFDA/ucm148722.htm> Accessed December, 2017
- FDA (2016) FDA Authority Over Cosmetics: How Cosmetics Are Not FDA-Approved, but Are FDA-Regulated. U.S. Food and Drug Administration (FDA). In. <https://www.fda.gov/Cosmetics/GuidanceRegulation/LawsRegulations/ucm074162.htm> Accessed October, 2017
- FDA (2017) Nail Care Products. U.S. Food and Drug Administration (FDA). In. <http://www.fda.gov/Cosmetics/ProductsIngredients/Products/ucm127068.htm#note> Accessed February, 2018
- FDA (2018) Milestones in U.S. Food and Drug Law History. In. <https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm2007256.htm> Accessed July, 2018
- Filley CM, Halliday W, Kleinschmidt-DeMasters BK (2004) The effects of toluene on the central nervous system. *Journal of neuropathology and experimental neurology* 63(1):1-12
- Fischman CM, Oster JR (1979) Toxic effects of toluene: A new cause of high anion gap metabolic acidosis. *JAMA* 241(16):1713-1715
- Foo SC, Jeyaratnam J, Koh D (1990) Chronic neurobehavioural effects of toluene. *Br J Ind Med* 47(7):480-484
- Ford AR (2014) "Overexposed, Underinformed": Nail Salon Workers and Hazards to Their Health / A Review of the Literature. National Network on Environments and Women's Health (NNEWH).

- Forkman BA, Ljungberg T, Johnson AC, et al. (1991) Long-term effects of toluene inhalation on rat behavior. *Neurotoxicol Teratol* 13(5):475-481
- Franke C, Studinger G, Berger G, et al. (1994) The assessment of bioaccumulation. *Chemosphere* 29(7):1501-1514
- Garcia E, Sharma S, Pierce M, et al. (2015) Evaluating a county-based healthy nail salon recognition program. *Am J Ind Med* 58(2):193-202 doi:10.1002/ajim.22379
- Gjølstad M, Thorud S, Molander P (2006) Occupational exposure to airborne solvents during nail sculpturing. *J Environ Monit* 8(5):537-542 doi:10.1039/b601917j
- Goldin LJ, Ansher L, Berlin A, et al. (2014) Indoor air quality survey of nail salons in Boston. *J Immigr Minor Health* 16(3):508-514 doi:10.1007/s10903-013-9856-y
- Goodwin TM (1988) Toluene abuse and renal tubular acidosis in pregnancy. *Obstet Gynecol* 71(5):715-718
- Gotohda T, Nishimura A, Morita K (2009) Immunohistochemical studies on early stage of hepatic damage induced by subacute inhalation of toluene vapor in rats. *J Appl Toxicol* 29(6):505-509 doi:10.1002/jat.1435
- Grandjean P, Landrigan PJ (2006) Developmental neurotoxicity of industrial chemicals. *Lancet* 368(9553):2167-2178 doi:10.1016/S0140-6736(06)69665-7
- Greenberg MM (1997) The central nervous system and exposure to toluene: A risk characterization. *Environ Res* 72(1):1-7 doi:10.1006/enrs.1996.3686
- Grešner P, Świercz R, Król MB, Twardowska E, Gromadzińska J, Wąsowicz W (2016) Does the Low-level occupational exposure to volatile organic compounds alter the seasonal variation of selected markers of oxidative stress? A case-control study in nail technicians. *Journal of Occupational Medicine and Toxicology* 11(36):1-11
- Grešner P, Świercz R, Wąsowicz W, Gromadzińska J (2017) Faster health deterioration among nail technicians occupationally exposed to low levels of volatile organic compounds. *Int J Occ Med and Env Health* 30(3):469-483
- GS1 (2017) Global Product Classification (GPC). In. <https://www.gs1.org/gpc/browser> Accessed October 2017 - February 2018
- Halliday-Bell JA, Gissler M, Jaakkola JJK (2009) Work as a hairdresser and cosmetologist and adverse pregnancy outcomes. *Occup Med (Lond)* 59(3):180-184 doi:10.1093/occmed/kqp017
- Hannigan JH, Bowen SE (2010) Reproductive toxicology and teratology of abused toluene. *Syst Biol Reprod Med* 56(2):184-200 doi:10.3109/19396360903377195
- Harris-Roberts J, Bowen J, Sumner J, et al. (2011) Work-related symptoms in nail salon technicians. *Occup Med (Lond)* 61(5):335-340 doi:10.1093/occmed/kqr096
- Hass U, Lund SP, Hougaard KS, Simonsen L (1999) Developmental neurotoxicity after toluene inhalation exposure in rats. *Neurotoxicol Teratol* 21(4):349-357
- Herdt-Losavio ML, Lin S, Druschel CM, Hwang SA, Mauer MP, Carlson GA (2009) The risk of having a low birth weight or preterm infant among cosmetologists in New York State. *Matern Child Health J* 13(1):90-97 doi:10.1007/s10995-008-0324-6
- Hersh JH (1989) Toluene embryopathy: Two new cases. *J Med Genet* 26:333-337
- Hersh JH, Podruch PE, Rogers G, Weisskopf B (1985) Toluene embryopathy. *J Pediatr* 106(6):922-927
- HHS (2017) Household Products Database, Health and Safety Information on Household Products. U.S Department of Health and Human Services (HHS), National Institute of Health, National Library of Medicine. In. <https://householdproducts.nlm.nih.gov/index.htm> Accessed September 2017
- Hillefors-Berglund M, Liu Y, von Euler G (1995) Persistent, specific and dose-dependent effects of toluene exposure on dopamine D₂ agonist binding in the rat caudate-putamen. *Toxicology* 100(1-3):185-194
- Hogie M, Guerbet M, Reber A (2009) The toxic effects of toluene on the optokinetic nystagmus in pigmented rats. *Ecotoxicol Environ Saf* 72(3):872-878 doi:10.1016/j.ecoenv.2008.02.016

- Hollund BE, Moen BE (1998) Chemical exposure in hairdresser salons: effect of local exhaust ventilation. *Ann Occup Hyg* 42(4):277-281
- Hougaard KS, Hass U, Lund SP, Simonsen L (1999) Effects of prenatal exposure to toluene on postnatal development and behavior in rats. *Neurotoxicol Teratol* 21(3):241-250
- Howard PH, ed. (1991) *Handbook of Environmental Degradation Rates*. CRC Press, Lewis Publishers Chelsea, MI [As described by ATSDR 2017]
- HSDB (2012) N-Butyl Acetate. Hazardous Substances Data Bank (HSDB). In. <https://toxnet.nlm.nih.gov/newtoxnet/hsdb.htm> Accessed October 2017
- HSDB (2015) Ethyl Acetate. Hazardous Substances Data Bank (HSDB). In. <https://toxnet.nlm.nih.gov/newtoxnet/hsdb.htm> Accessed October 2017
- HSDB (2016) Toluene. Hazardous Substances Data Bank (HSDB). In. <https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?./temp/~B9AijZ:3> Accessed July - October 2017
- Hsieh GC, Parker RDR, Sharma RP, Hughes BJ (1990) Subclinical effects of groundwater contaminants. III. Effects of repeated oral exposure to combinations of benzene and toluene on immunologic responses in mice. *Arch Toxicol* 64(4):320-328
- Hsieh GC, Sharma RP, Parker RDR (1989) Immunotoxicological evaluation of toluene exposure via drinking water in mice. *Environ Res* 49(1):93-103
- Hsieh GC, Sharma RP, Parker RDR (1991) Hypothalamic-pituitary-adrenocortical axis activity and immune function after oral exposure to benzene and toluene. *Immunopharmacology* 21(1):23-32
- Huerta-Rivas A, López-Rubalcava C, Sánchez-Serrano SL, Valdez-Tapia M, Lamas M, Cruz SL (2012) Toluene impairs learning and memory, has antinociceptive effects, and modifies histone acetylation in the dentate gyrus of adolescent and adult rats. *Pharmacol Biochem Behav* 102(1):48-57
- IARC (1999) IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 71. Re-evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide. Toluene. International Agency for Research on Cancer (IARC)
- IPCS (2005) Concise International Chemical Assessment, Document 64. Butyl Acetates. International Programme on Chemical Safety (IPCS). In. <http://www.inchem.org/documents/cicads/cicads/cicad64.htm> Accessed October 2017
- John EM, Savitz DA, Shy CM (1994) Spontaneous abortions among cosmetologists. *Epidemiology* 5(2):147-155
- Kamijima M, Nakazawa Y, Yamakawa M, et al. (1994) Metabolic acidosis and renal tubular injury due to pure toluene inhalation. *Arch Environ Health* 49:410-413
- Kang SK, Rohlman DS, Lee MY, Lee HS, Chung SY, Anger WK (2005) Neurobehavioral performance in workers exposed to toluene. *Environ Toxicol Pharmacol* 19(3):645-650 doi:10.1016/j.etap.2004.12.049
- Killus JP, Whitten GZ (1982) A mechanism describing the photochemical oxidation of toluene in smog. *Atmospheric Environment* (1967) 16(8):1973-1988 doi:[https://doi.org/10.1016/0004-6981\(82\)90468-1](https://doi.org/10.1016/0004-6981(82)90468-1)
- Kim DB, Lee JK, Jung KJ, Yoon YP (1998) Effects of toluene inhalation on the concentrations of the brain monoamines and metabolites. *J Toxicol Pub Health* 14(4):495-500
- Kishi R, Harabuchi I, Ikeda T, Yokota H, Miyake H (1988) Neurobehavioral effects and pharmacokinetics of toluene in rats and their relevance to man. *Br J Ind Med* 45(6):396-408
- Kiyokawa M, Mizota A, Takasoh M, Adachi-Usami E (1999) Pattern visual evoked cortical potentials in patients with toxic optic neuropathy caused by toluene abuse. *Jpn J Ophthalmol* 43(5):438-442
- Kodavanti PRS, Royland JE, Moore-Smith DA, et al. (2015) Acute and subchronic toxicity of inhaled toluene in male Long-Evans rats: Oxidative stress markers in brain. *Neurotoxicology* 51:10-19 doi:10.1016/j.neuro.2015.09.001
- Kopelovich L, Perez AL, Jacobs N, Mendelsohn E, Keenan JJ (2015) Screening-level human health risk assessment of toluene and dibutyl phthalate in nail lacquers. *Food Chem Toxicol* 81:46-53 doi:10.1016/j.fct.2015.04.011

- Kroeger RM, Moore RJ, Lehman TH, Giesy JD, Skeeters CE (1980) Recurrent urinary calculi associated with toluene sniffing. *J Urol* 123(1):89-91
- Kronevi T, Wahlberg J, Holmberg B (1979) Histopathology of skin, liver, and kidney after epicutaneous administration of five industrial solvents to guinea pigs. *Environ Res* 19(1):56-69
- Laslo-Baker D, Barrera M, Knittel-Keren D, et al. (2004) Child neurodevelopmental outcome and maternal occupational exposure to solvents. *Arch Pediatr Adolesc Med* 158(10):956-961
doi:10.1001/archpedi.158.10.956
- Leeder JS, Kearns GL (1997) Pharmacogenetics in pediatrics. Implications for practice. *Pediatr Clin North Am* 44(1):55-77
- Lindemann R (1991) Congenital renal tubular dysfunction associated with maternal sniffing of organic solvents. *Acta Pediatr Scand* 80(8-9):882-884
- López-Rubalcava C, Hen R, Cruz SL (2000) Anxiolytic-like actions of toluene in the burying behavior and plus-maze tests: Differences in sensitivity between 5-HT_{1B} knockout and wild-type mice. *Behav Brain Res* 115(1):85-94
- LoSasso GL, Rapport LJ, Axelrod BN (2001) Neuropsychological symptoms associated with low-level exposure to solvents and (meth)acrylates among nail technicians. *Neuropsychiatry Neuropsychol Behav Neurol* 14(3):183-189
- LoSasso GL, Rapport LJ, Axelrod BN, Whitman RD (2002) Neurocognitive sequelae of exposure to organic solvents and (meth)acrylates among nail-studio technicians. *Neuropsychiatry Neuropsychol Behav Neurol* 15(1):44-55
- Malnou A (2014) Water-based nail-polish composition. U.S. Patent No. US 8,883,126 B2. France Patent,
- Marlow DA, Looney T, Reutman S (2012) An Evaluation of Local Exhaust Ventilation Systems for Controlling Hazardous Exposures in Nail Salons. EPHB Report No. 005-164. Centers for Disease Control and Prevention (CDC), National Institute for Occupational Safety and Health (NIOSH), Division of Applied Research and Technology, Engineering and Physical Hazards Branch (EPHB)
- Mayer AS, Brazile WJ, Erb S, Autenrieth DA, Serrano K, Van Dyke MV (2015) Developing effective worker health and safety training materials: Hazard awareness, identification, recognition, and control for the salon industry. *J Occup Environ Med* 57(5):537-542 doi:10.1097/JOM.0000000000000400
- McNary JE, Jackson EM (2007) Inhalation exposure to formaldehyde and toluene in the same occupational and consumer setting. *Inhal Toxicol* 19(6-7):573-576 doi:10.1080/08958370701270946
- McWilliams ML, Chen GD, Fechter LD (2000) Low-level toluene disrupts auditory function in guinea pigs. *Toxicol Appl Pharmacol* 167(1):18-29 doi:10.1006/taap.2000.8978
- Meulenbelt J, de Groot G, Savelkoul TJF (1990) Two cases of acute toluene intoxication. *Br J Ind Med* 47(6):417-420
- Miller MD, Marty MA, Arcus A, Brown J, Morry D, Sandy M (2002) Differences between children and adults: Implications for risk assessment at California EPA. *International Journal of Toxicology* 21:403-418
doi:10.1080/1091581029009663
- Mintel (2018) Mintel's Global New Products Database. In. <http://www.mintel.com/global-new-products-database> Accessed January, 2018
- Mullin LS, Krivanek ND (1982) Comparison of unconditioned reflex and conditioned avoidance tests in rats exposed by inhalation to carbon monoxide, 1,1,1-trichloroethane, toluene or ethanol. *Neurotoxicology* 3(1):126-137
- Muttray A, Wolters V, Jung D, Konietzko J (1999) Effects of high doses of toluene on color vision. *Neurotoxicol Teratol* 21(1):41-45
- Nails Magazine (2015) Industry Statistics Highlights. In: 2014-2015 Nails Big Book. <http://www.nailsmag.com/page/70218/market-research> Accessed September 2017
- Nails Magazine (2016) 2015-2016 Nails The Big Book. In. <http://files.nailsmag.com/Feature-Articles-in-PDF/NABB2015-16stats.pdf> Accessed October, 2017

- Nails Magazine (2017) 2016-2017 Industry Statistics. In: 2016-2017 Nails The Big Book. <http://www.nailsmag.com/page/70218/market-research> Accessed September, 2017
- Nakajima T, Wang RS, Katakura Y, et al. (1992) Sex-, age- and pregnancy-induced changes in the metabolism of toluene and trichloroethylene in rat liver in relation to the regulation of cytochrome P450IIE1 and P450IIC11 content. *J Pharmacol Exp Ther* 261(3):869-874
- Nelson BK, Brightwell WS, MacKenzie-Taylor DR, et al. (1988) Teratogenicity of n-propanol and isopropanol administered at high inhalation concentrations to rats. *Food Chem Toxicol* 26(3):247-254
- Nguyen C (2016) Indoor air quality of nail salons in the greater Los Angeles area: Assessment of chemical and particulate matter exposures and ventilation. Thesis UCLA, UCLA
- NIOSH (1999) Controlling Chemical Hazards During the Application of Artificial Fingernails. National Institute for Occupational Safety and Health (NIOSH). In: <https://www.cdc.gov/niosh/docs/99-112/pdfs/99-112.pdf> Accessed July, 2017
- NIOSH (2016) Workplace Safety & Health Topics, Hierarchy of Controls. The National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention. In: <https://www.cdc.gov/niosh/topics/hierarchy/> Accessed April, 2018
- NTP (1990) Toxicology and Carcinogenesis Studies of Toluene (CAS No. 108-88-3) in F344/N Rats and B6C3F₁ Mice (Inhalation Studies). Technical Report Series No. 371. NIH Publication No. 90-2826. National Toxicology Program (NTP)
- NYSDOH (2016) Review of Chemicals Used in Nail Salons. New York State Department of Health (NYSDOH)
- O'Brien ET, Yeoman WB, Hobby JAE (1971) Hepatorenal damage from toluene in a "glue sniffer". *Br Med J* 2(752):29-30
- OEHHA (1991) Chemicals Known to the State to Cause Cancer or Reproductive Toxicity (Prop 65 List). Office of Environmental Health Hazard Assessment (OEHHA). In: http://www.dtsc.ca.gov/SCP/upload/1-A-Prop65list_04-19-13.pdf Accessed July 2017
- OEHHA (1999) Public Health Goal for Toluene In Drinking Water. February 1999. Office of Environmental Health Hazard Assessment (OEHHA)
- OEHHA (2008) Air Toxics Hot Spots Risk Assessment Guidelines, Technical Support Document For the Derivation of Noncancer Reference Exposure Levels (RELs), Appendix D.2 Acute RELs and toxicity summaries using the previous version of the Hot Spots Risk Assessment guidelines (OEHHA 1999). Office of Environmental Health Hazard Assessment (OEHHA)
- OEHHA (2016) Acute, 8-hour and Chronic Reference Exposure. Office of Environmental Health Hazard Assessment (OEHHA). In: <http://www.dtsc.ca.gov/SCP/upload/2-E-CA-RELs.pdf> Accessed July, 2017
- Ono A, Sekita K, Ohno K, et al. (1995) Reproductive and developmental toxicity studies of toluene. I. Teratogenicity study of inhalation exposure in pregnant rats. *J Toxicol Sci* 20(2):109-134
- Ørbæk P, Nise G (1989) Neurasthenic complaints and psychometric function of toluene-exposed rotogravure printers. *Am J Ind Med* 16(1):67-77
- Ørbæk P, Österberg K, Åkesson B, Bergendorf U, Karlson B, Seger L (1998) Suprathreshold intensity and annoyance reactions in experimental challenge to toluene and n-butyl acetate among subjects with long-term solvent exposure. *Scand J Work Environ Health* 24(5):432-438 doi:10.5271/sjweh.366
- OSHA (1993) 29 CFR Part 1910. Air contaminants. Federal Register 58:35338-35351. In: Occupational Safety and Health Administration (OSHA). <https://www.osha.gov/laws-regs/federalregister/1993-06-30-0> Accessed October, 2017
- OSHA (2012) Stay Healthy and Safe While Giving Manicures and Pedicures. A Guide for Nail Salon Workers. Occupational Safety and Health Administration (OSHA)
- OSHA (2017) Health Hazards in Nail Salons. Occupational Safety and Health Administration (OSHA). In: <https://www.osha.gov/SLTC/nailsalons/chemicalhazards.html#steps> Accessed October, 2017
- OSHA (2018a) Permissible Exposure Limits – Annotated Tables. Occupational Safety and Health Administration (OSHA). In: <https://www.osha.gov/dsg/annotated-pels/> Accessed January, 2018

- OSHA (2018b) Toluene. Occupational Exposure Limits. Occupational Safety and Health Administration (OSHA). In. https://www.osha.gov/SLTC/toluene/exposure_limits.html Accessed January, 2018
- OSHSB (2012) Airborne Contaminants. General Industry Safety Orders, Division 1, Chapter 4, Subchapter 7, Article 107, Section 5155. Occupational Safety & Health Standards Board (OSHSB). In. http://www.dir.ca.gov/oshsb/Airborne_Contaminants_2011.html January 2018
- Österberg K, Ørbæk P, Karlson B, Åkesson B, Bergendorf U (2003) Annoyance and performance during the experimental chemical challenge of subjects with multiple chemical sensitivity. *Scand J Work Environ Health* 29(1):40-50 doi:10.5271/sjweh.703
- Páez-Martínez N, Ambrosio E, García-Lecumberri C, Rocha L, Montoya GL, Cruz SL (2008) Toluene and TCE decrease binding to mu-opioid receptors, but not to benzodiazepine and NMDA receptors in mouse brain. *Ann N Y Acad Sci* 1139:390-401
- Páez-Martínez N, Cruz SL, López-Rubalcava C (2003) Comparative study of the effects of toluene, benzene, 1,1,1-trichloroethane, diethyl ether, and flurothyl on anxiety and nociception in mice. *Toxicol Appl Pharmacol* 193(1):9-16
- Pak VM, Powers M, Liu J (2013) Occupational chemical exposures among cosmetologists: Risk of reproductive disorders. *Workplace Health & Safety* 61(12):522-528
- Park SA, Gwak S, Choi S (2014) Assessment of occupational symptoms and chemical exposures for nail salon technicians in Daegu City, Korea. *J Prev Med Public Health* 47(3):169-176 doi:10.3961/jpmph.2014.47.3.169
- Pearson MA, Hoyme HE, Seaver LH, Rimsza ME (1994) Toluene embryopathy: Delineation of the phenotype and comparison with fetal alcohol syndrome. *Pediatrics* 93(2):211-215
- Peters LI, Hawker D, Bartkow ME, Tapper S, Gore W (2007) Indoor air concentrations of various volatile organic compounds in a suburban nail salon. *Clean Air and Environmental Quality* 41(1):39-42
- Pierce CH, Chen Y, Dills RL, Kalman DA, Morgan MS (2002) Toluene metabolites as biological indicators of exposure. *Toxicology Letters* 129(1):65-76 doi:[https://doi.org/10.1016/S0378-4274\(01\)00472-6](https://doi.org/10.1016/S0378-4274(01)00472-6)
- Pryor GT, Rebert CS, Dickinson J, Feeney EM (1984) Factors affecting toluene-induced ototoxicity in rats. *Neurobehav Toxicol Teratol* 6(3):223-238
- Quach T, Gunier R, Tran A, et al. (2011) Characterizing workplace exposures in Vietnamese women working in California nail salons. *Am J Public Health* 101 Suppl 1(Supplement 1):S271-S276 doi:10.2105/AJPH.2010.300099
- Quach T, Liou J, Fu L, Mendiratta A, Tong M, Reynolds P (2012) Developing a proactive research agenda to advance nail salon worker health, safety, and rights. *Prog Community Health Partnersh* 6(1):75-82 doi:10.1353/cpr.2012.0005
- Quach T, Nguyen KD, Doan-Billings PA, Okahara L, Fan C, Reynolds P (2008) A preliminary survey of Vietnamese nail salon workers in Alameda County, California. *J Community Health* 33(5):336-343 doi:10.1007/s10900-008-9107-7
- Quach T, Varshavsky J, Von Behren J, et al. (2013) Reducing chemical exposures in nail salons through owner and worker trainings: An exploratory intervention study. *American Journal of Industrial Medicine* 56:806-817 doi:10.1002/ajim.22146
- Rister R (2016) Health Problems Caused by Biting Painted Nails are Not Limited to Chemical Toxicity. In: SteadyHealthcom. <https://www.steadyhealth.com/articles/can-you-poison-yourself-by-biting-your-nails-toxic-chemicals-abound-in-most-brands-of-nail-polish/health-problems-caused-by-biting-painted-nails-are-not-limited-to-chemical-toxicity> Accessed April, 2018
- Roberts LG, Bevans AC, Schreiner CA (2003) Developmental and reproductive toxicity evaluation of toluene vapor in the rat. I. Reproductive toxicity. *Reproductive toxicology* (Elmsford, NY) 17(6):649-658 doi:10.1016/s0890-6238(03)00106-0

- Roberts LG, Nicolich MJ, Schreiner CA (2007) Developmental and reproductive toxicity evaluation of toluene vapor in the rat II. Developmental toxicity. *Reproductive toxicology* (Elmsford, NY) 23(4):521-531 doi:10.1016/j.reprotox.2007.01.009
- Roelofs C, Azaroff LS, Holcroft C, Nguyen H, Doan T (2008) Results from a community-based occupational health survey of Vietnamese-American nail salon workers. *J Immigr Minor Health* 10(4):353-361 doi:10.1007/s10903-007-9084-4
- Roelofs C, Do T (2012) Exposure assessment in nail salons: An indoor air approach. *ISRN Public Health* 2012:1-7 doi:10.5402/2012/962014
- Roelofs C, Do T, Truong T (2007) "Indoor Air Quality in Nail Salons." Presentation, American Industrial Hygiene Conference and Exhibition. June 6, 2007. Philadelphia, PA
- Romanowski S (2015) The trends polishing up the nail care market. Mintel. In. <http://www.mintel.com/blog/beauty-market-news/the-trends-polishing-up-the-us-nail-care-market> Accessed September, 2017
- Saito A, Tanaka H, Usuda H, et al. (2011) Characterization of skin inflammation induced by repeated exposure of toluene, xylene, and formaldehyde in mice. *Environmental toxicology* 26(3):224-232 doi:10.1002/tox.20547
- Sally Beauty Supply (2017) How often should I get a professional manicure? In. https://www.sallybeauty.com/FAQ_NAILS_048.html Accessed December, 2017
- Samuel-Herter SR, Slaght SL, McKay BE (2014) Age-dependent time courses of recovery for motor functions following acute toluene intoxication in rats. *Dev Psychobiol* 56(4):657-673 doi:10.1002/dev.21134
- Sato A, Nakajima T (1978) Differences following skin or inhalation exposure in the absorption and excretion kinetics of trichloroethylene and toluene. *Br J Ind Med* 35(1):43-49
- SCCP (2008) Opinion on Toluene (its use as a solvent in nail cosmetics). Scientific Committee on Consumer Products (SCCP), European Commission
- Schikler KN, Lane EE, Seitz K, Collins WM (1984) Solvent abuse associated pulmonary abnormalities. *Adv Alcohol Subst Abuse* 3(3):75-81 doi:10.1300/J251v03n03_07
- SF Environment (2017) Email communication from Megan Kalsman of San Francisco Department of the Environment (SF Environment) to Dicle Yardimci of DTSC on July 5, 2017.
- SF Environment (2018) Healthy Nail Salon Program. San Francisco Department of the Environment (SF Environment). In. <https://sfenvironment.org/article/healthy-nail-salon-program> Accessed March, 2018
- Shendell DG, Graber JM, Milich LJ, Pratt ME (2018) Assessing acute symptoms related to occupational exposures among nail salon technicians. *J Occup Environ Med* 60(4):343-349 doi:10.1097/JOM.0000000000001210
- Shibata K, Yoshita Y, Matsumoto H (1994) Extensive chemical burns from toluene. *Am J Emerg Med* 12(3):353-355
- Soberanes-Chávez P, López-Rubalcava C, de Gortari P, Cruz SL (2013) Exposure to toluene and stress during pregnancy impairs pups' growth and dams' lactation. *Neurotoxicol Teratol* 40:9-16 doi:10.1016/j.ntt.2013.07.011
- Statista (2017a) U.S. population: Do you use nail polish / nail care products? In. <https://www.statista.com/statistics/276463/us-households-usage-of-nail-polish-and-nail-care-products/> Accessed December, 2017
- Statista (2017b) U.S. population: Usage of nail polish / nail care products from 2011 to 2020. In. <https://www.statista.com/statistics/286905/usage-nail-polish-nail-care-products-us-trend/> Accessed December, 2017
- Streicher HZ, Gabow PA, Moss AH, Kono D, Kaehny WD (1981) Syndromes of toluene sniffing in adults. *Ann Intern Med* 94(6):758-762
- SWRCB (2012) Final 2012 California Integrated Report (Clean Water Act Section 303(d) List / 305(b) Report). State Water Resources Control Board (SWRCB). In.

- http://www.waterboards.ca.gov/water_issues/programs/tmdl/integrated2012.shtml Accessed July 2017
- SWRCB (2014) Maximum Contaminant Levels and Regulatory Dates for Drinking Water, U.S. EPA vs. California. State Water Resources Control Board (SWRCB). In. http://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/documents/dwdocuments/MCLsEPAsDWP-2014-07-01.pdf Accessed July 2017
- Taher SM, Anderson RJ, McCartney R, Popovtzer MM, Schrier RW (1974) Renal tubular acidosis associated with toluene “sniffing”. *N Engl J Med* 290(14):765-768
- Tähti H, Aaran RK, Vapaatalo H (1983) An inhalation method for testing the toxicity of volatile compounds in small laboratory animals. A study on short-term and long-term toluene inhalation in rats. *Meth Find Exp Clin Pharmacol* 5(10):667-671
- Tardif R, Laparé S, Plaa GL, Brodeur J (1991) Effect of simultaneous exposure to toluene and xylene on their respective biological exposure indices in humans. *Int Arch Occup Environ Health* 63:279-284
- Tardif R, Plaa GL, Brodeur J (1992) Influence of various mixtures of inhaled toluene and xylene on the biological monitoring of exposure to these solvents in rats. *Can J Physiol Pharmacol* 70:385-393
- Taylor JD, Evans HL (1985) Effects of toluene inhalation on behavior and expired carbon dioxide in macaque monkeys. *Toxicol Appl Pharmacol* 80(3):487-495
- Tomaszycki ML, Aulerich KE, Bowen SE (2013) Repeated toluene exposure increases c-Fos in catecholaminergic cells of the nucleus accumbens shell. *Neurotoxicol Teratol* 40:28-34 doi:10.1016/j.ntt.2013.09.001
- Tsigonis A, Lagoudi A, Chandrinou S, Linos A, Evlogias N, Alexopoulos EC (2010) Indoor air in beauty salons and occupational health exposure of cosmetologists to chemical substances. *Int J Environ Res Public Health* 7(1):314-324 doi:10.3390/ijerph7010314
- U.S. EPA (2018) TSCA Chemical Substance Inventory. In. <https://www.epa.gov/tsca-inventory/how-access-tsca-inventory#download> Accessed July, 2018
- U.S. Census Bureau (2012) Survey of Business Owners (SBO) - Characteristics of Businesses: 2012 Tables. In. https://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?pid=SBO_2012_00CSA01&prodType=table Accessed October, 2017
- U.S. EPA (2000) Section 131.38 of title 40 of the Code of Federal Regulations. Establishment of numeric criteria for priority toxic pollutants for the State of California. Environmental Protection Agency (EPA).
- U.S. EPA (2003) Toxicological Review of Methyl Ethyl Ketone (CAS No. 78-93-3) In Support of Summary Information on the Integrated Risk Information System (IRIS). U.S. Environmental Protection Agency
- U.S. EPA (2005a) Integrated Risk Information System (IRIS), Chemical Assessment Summary, Toluene; CASRN 108-88-3. U.S. Environmental Protection Agency (U.S. EPA). In. https://cfpub.epa.gov/ncea/iris/iris_documents/documents/subst/0118_summary.pdf Accessed July 2017
- U.S. EPA (2005b) Toxicological Review of Toluene (CAS No. 108-88-3) In Support of Summary Information on the Integrated Risk Information System (IRIS). U. S. Environmental Protection Agency (U.S. EPA)
- U.S. EPA (2007) Protecting the Health of Nail Salon Workers. U.S. Environmental Protection Agency (U.S. EPA)
- U.S. EPA (2011) Exposure Factors Handbook: 2011 Edition. U.S. Environmental Protection Agency (U.S. EPA), Washington, DC
- U.S. EPA (2012) Toluene - Factsheet. U. S. Environmental Protection Agency (U.S. EPA). In. <https://www.epa.gov/sites/production/files/2016-09/documents/toluene.pdf> Accessed January 2018
- U.S. EPA (2018) U.S. EPA ChemView, Chemical Data Reporting. U.S. Environmental Protection Agency (U.S. EPA). In. <https://chemview.epa.gov/chemview> Accessed October, 2017
- Uaki H, Kawai T, Mizunuma K, et al. (1995) Dose-dependent suppression of toluene metabolism by isopropyl alcohol and methyl ethyl ketone after experimental exposure of rats. *Toxicol Lett* 81(2-3):229-234
- Ungváry G, Tátrai E (1985) On the embryotoxic effects of benzene and its alkyl derivatives in mice, rats and rabbits. *Arch Toxicol Suppl* 8:425-430

- Ungváry G, Tátrai E, Szeberényi S, Rodics K, Lorincz M, Barcza G (1982) Effect of toluene exposure on the liver under different experimental conditions. *Exp Mol Pathol* 36(3):347-360
- Vieira I, Sonnier M, Cresteil T (1996) Developmental expression of CYP2E1 in the human liver. Hypermethylation control of gene expression during the neonatal period. *Eur J Biochem* 238(2):476-483
- von Euler G, Ogren SO, Li XM, Fuxe K, Gustafsson JA (1993) Persistent effects of subchronic toluene exposure on spatial learning and memory, dopamine-mediated locomotor activity and dopamine D₂ agonist binding in the rat. *Toxicology* 77(3):223-232
- Vural M, Ogel K (2006) Dilated cardiomyopathy associated with toluene abuse. *Cardiology* 105(3):158-161 doi:10.1159/000091344
- Wang RS, Nakajima T, Tsuruta H, Honma T (1996) Effect of exposure to four organic solvents on hepatic cytochrome P450 isozymes in rat. *Chem Biol Interact* 99(1-3):239-252
- Weschler CJ, Nazaroff WW (2014) Dermal uptake of organic vapors commonly found in indoor air. *Environmental science & technology* 48(2):1230-1237 doi:10.1021/es405490a
- White H, Khan K, Lau C, Leung H, Montgomery D, Rohlman DS (2015) Identifying health and safety concerns in Southeast Asian immigrant nail salon workers. *Arch Environ Occup Health* 70(4):196-203 doi:10.1080/19338244.2013.853644
- WHO (2000) Air Quality Guidelines for Europe. Second edition. World Health Organization (WHO) Regional Publications, European Series, No. 91, Denmark
- Wilkins-Haug L, Gabow PA (1991) Toluene abuse during pregnancy: Obstetric complications and perinatal outcomes. *Obstet Gynecol* 77(4):504-509
- Win-Shwe TT, Fujimaki H (2010) Neurotoxicity of toluene. *Toxicol Lett* 198(2):93-99 doi:10.1016/j.toxlet.2010.06.022
- Win-Shwe TT, Kunugita N, Yoshida Y, Nakajima D, Tsukahara S, Fujimaki H (2012) Differential mRNA expression of neuroimmune markers in the hippocampus of infant mice following toluene exposure during brain developmental period. *J Appl Toxicol* 32(2):126-134 doi:10.1002/jat.1643
- Wolf K (2016) Safer Alternative Nail Polish Removers for Salons and Consumers. Prepared for: Paul H. Johanson Fund, Bay Area Air Quality Management District. Institute for Research and Technical Assistance
- Wolf MA, Rowe VK, McCollister DD, Hollingsworth RL, Oyen F (1956) Toxicological studies of certain alkylated benzenes and benzene. Experiments on laboratory animals. *AMA archives of industrial health* 14(4):387-398
- Wood RW, Colotla VA (1990) Biphasic changes in mouse motor activity during exposure to toluene. *Fundam Appl Toxicol* 14(1):6-14
- Wood RW, Rees DC, Laties VG (1983) Behavioral effects of toluene are modulated by stimulus control. *Toxicol Appl Pharmacol* 68(3):462-472
- Wu XM, Bennett DH, Ritz B, Cassady DL, Lee K, Hertz-Picciotto I (2010) Usage pattern of personal care products in California households. *Food Chem Toxicol* 48(11):3109-3119 doi:10.1016/j.fct.2010.08.004
- Yang JH, Han DH (2010) Occupational exposure of nail technicians to airborne chemicals and biological monitoring. *J Korean Soc Occup Environ Hyg* 20(1):53-62
- Zavalic M, Mandic Z, Turk R, Bogadi-Sare A, Plavec D (1998) Quantitative assessment of color vision impairment in workers exposed to toluene. *Am J Ind Med* 33(3):297-304
- Zhou W, Wang PG, Wittenberg JB, Rua D, Krynskiy AJ (2016) Simultaneous determination of cosmetics ingredients in nail products by fast gas chromatography with tandem mass spectrometry. *J Chromatogr A* 1446:134-140 doi:10.1016/j.chroma.2016.04.003

APPENDIX 1 – REPORT PREPARATION

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